#### **RESEARCH ARTICLE**



# Epidemiology of Vascular Thrombosis in the Eastern Province of Saudi Arabia: A Single Center Study and Comparison with National Data

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## Abstract

**Background** Despite the growing evidence on the thrombophilia in Saudi population along its diverse regions, there have been no studies on thrombotic events in the Eastern Province of Saudi Arabia. This single-center study aimed to investigate the prevalence of venous thromboembolism (VTE) in a hematology clinic in the Eastern Province of Saudi Arabia between January 2015 and May 2023. The objective of this study was to investigate the clinical characteristics of VTE and compare them with national data.

**Methods** This is a retrospective, observational, single-center study conducted in the Eastern Province from January 2015 to May 2023. After applying the inclusion and exclusion criteria and the prevalence rate calculation an analysis of n = 170 patients was conducted to compare the epidemiological results of the current study with national data published in other provinces of Saudi Arabia. Data collected included demographics, comorbidities and location with thrombosis recurrence. **Result** The prevalence rate of VTE in this cohort was 3.16%. Women made up 70% of the population. About 80.5% of cases were obese or overweight, 37.6% of cases had comorbidities that may increase the risk of thrombosis, and 12.9% of cases were associated with smoking. The most common site of VTE (56.5%) and the site of higher recurrence of VTE (21.8%) was the lower extremities. In addition, recurrent VTE was observed in 28.2% of cases, reflecting a significantly higher recurrence rate compared with other national studies (p = 0.001). Compared with other national statistics, the most significant risk factors for thrombosis in the Eastern Province were smoking, obesity and family history (p = 0.000). Compared with national statistics, this study demonstrated significantly higher rates of VTE in pregnancy, patients on hormonal therapy, and patients with rheumatological/autoimmune diseases (p = 0.001).

**Conclusion** The incidence of VTE can be reduced by changing lifestyles and creating educational programs to educate people about the dangers of obesity and smoking.

Keywords Venous thromboembolism · Arterial thrombosis · Pulmonary embolism · Autoimmune disease · Prevalence

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## 1 Introduction

The development of a partial or total blood clot in the veins or arteries that results in clinical symptoms is known as thrombosis. The location and size of the thrombus determine the clinical manifestations which can range from mild to fatal [1]. Three factors, referred to as Virchow's triad, have historically contributed to the formation of thrombosis: endothelial damage to the vessel wall; blood stasis; and hypercoagulable state [2].

The hypercoagulable state, also known as thrombophilia, is a disorder with an increased tendency to form blood clots (thrombosis) due to the presence of one or more predisposing factors, which may be inherited or acquired [1–3]. Inherited forms are rare. A much more common occurrence is acquired hypercoagulability, which can be caused by chronic inflammatory diseases (e.g., rheumatological diseases, inflammatory bowel disease, surgery, pregnancy or infection), hormonal agents (e.g., oral contraceptives, estrogen or other hormone replacement drugs), or both [1–3]. In addition, COVID-19 infection and certain vaccinations have recently been linked to thromboembolism events [4, 5]. In essence, thrombophilia is a predisposition to develop venous thromboembolism (VTE) due to an underlying hypercoagulable state caused by inherited or acquired disorders of coagulation or fibrinolysis. Inherited disorders include deficiencies of natural anticoagulants such as antithrombin, protein C, protein S, elevated levels of coagulation factors (especially factor VIII), and prothrombotic polymorphisms in the genes encoding factor V (i.e. factor V Leiden) and prothrombin. Acquired conditions mainly include antiphospholipid antibody syndrome, malignancies, acquired increase in coagulation factors or acquired decrease in natural inhibitors, and hyperhomocysteinemia [6-9]. In terms of demographics, in particular, age groups have different prevalence rates. Thus, in reproductive age it is 1 in 10,000, and in older people it can reach 1 in 100 [1]. The incidence of thrombosis is estimated to be as high as 2 per 1000 person-years in Europe, the USA and South Korea, but lower in Asia and Africa [6–9].

In the Kingdom of Saudi Arabia, despite sporadic data and research efforts, there is currently no thrombosis registry. On the other hand, although the exact prevalence of deep vein thrombosis (DVT) in Saudi Arabia is unknown, it is estimated that 25,000 people suffer from thrombosis [10]. Data from King Fahd Medical City (KFMC, Riyadh) showed that 58% of cases were unprovoked and mostly involved females [11]. The results of the epidemiological study on thrombosis at Asir Hospital showed that hospital-acquired thrombosis predominated, occurring with

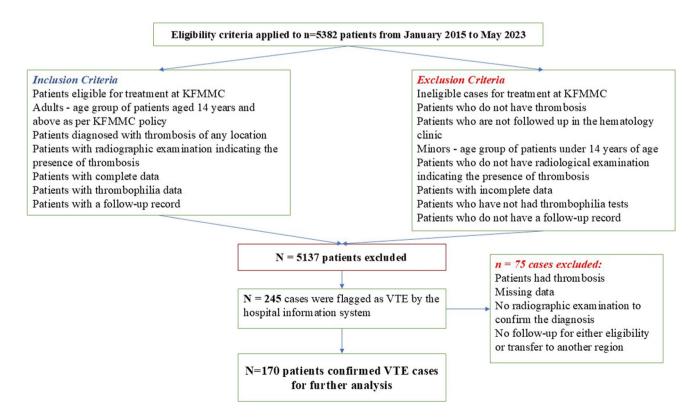


Fig. 1 Flow chart of application of eligibility criteria to study sample identification and analysis

a frequency of 18 cases in every 10,000 hospitalizations [12]. In addition, DVT was found to be highly prevalent (27.56%) in Al Madinah particularly in females [13]. Lastly, a multicenter study conducted in the southern region of Saudi Arabia found a high incidence of pulmonary embolism (PE) and DVT in immobilized patients who also had obesity and chronic diseases [14].

Despite the growing evidence on the thrombophilia in Saudi population along its diverse regions, there have been no studies on thrombotic events in the Eastern Province of Saudi Arabia, the largest province by area and the third most populous after the Riyadh and Mecca provinces. Moreover, the Eastern Province is considered the most obese region (29.4%), followed by Riyadh (26.9%), while the lowest was Baha (14.3%) [15]. Thus, based on this evidence, data gaps, and to improve the understanding of the disease and implications of genetic and environmental dissemination the aim of this study was developed. This single-center study aimed to investigate the prevalence of VTE in a hematology clinic in the Eastern Province of Saudi Arabia between January 2015 and May 2023. The objective of this study was to investigate the clinical characteristics of VTE and compare them with national data.

#### 2 Methods

### 2.1 Study Design and Setting

This retrospective observational study was conducted at a tertiary care hospital of King Fahd Military Medical Complex (KFMMC) among n = 170 patients seen in the outpatient clinic between January 2015 and May 2023 who were diagnosed with arterial or venous thrombosis, or both. KFMMC is a tertiary care government hospital and the most modern medical facility among the hospitals of the Ministry of Defense with 350 beds. It serves military personnel, their dependents, hospital staff and other beneficiaries in the Eastern Province, which provides a variety of data collection opportunities.

#### 2.2 Aim and Objective of the Study

This single-center study aimed to investigate the prevalence of VTE in a hematology clinic in the Eastern Province of Saudi Arabia between January 2015 and May 2023. The objective of this study was to investigate the clinical characteristics of VTE and compare them with national data. 
 Table 1
 Demographic and clinical characters

| Demographic an | nd clinical characters |  |
|----------------|------------------------|--|

| Age         | М        | in          | Max | M(SD)           |
|-------------|----------|-------------|-----|-----------------|
|             | 14       |             | 86  | 42.21 (±13.022) |
|             | Fr       | equency (N) |     | Percentage (%)  |
| Gender      |          |             |     |                 |
| Male        | 51       |             |     | 30              |
| Female      | 119      |             |     | 70              |
| Smoking     |          |             |     |                 |
| Yes         | 22       |             |     | 12.9            |
| No          | 148      |             |     | 87.1            |
| Family hist | ory      |             |     |                 |
| Yes         | 23       |             |     | 13.5            |
| No          | 147      |             |     | 86.5            |
| Comorbidit  | ty       |             |     |                 |
| Yes         | 64       |             |     | 37.6            |
| No          | 106      |             |     | 62.4            |
| Diabetes m  | ellitus  |             |     |                 |
| Yes         | 29       |             |     | 17              |
| No          | 141      |             |     | 82.9            |
| HTN         |          |             |     |                 |
| Yes         | 32       |             |     | 18.8            |
| No          | 138      |             |     | 81.1            |
| DLP         |          |             |     |                 |
| Yes         | 27       |             |     | 15.9            |
| No          | 143      |             |     | 84.1            |
| Cardiac     |          |             |     |                 |
| Yes         | 17       |             |     | 10              |
| No          | 153      |             |     | 90              |
| Renal       |          |             |     |                 |
| Yes         | 13       |             |     | 7.6             |
| No          | 157      |             |     | 92.4            |
| Hepatic     |          |             |     |                 |
| Yes         | 4        |             |     | 2.4             |
| No          | 166      |             |     | 97.6            |
| Obesity/ove | erweight |             |     |                 |
|             | 137      |             |     | 80.50           |

#### 2.3 Study Sample

Sample size determination was based on the formula for Proportion (Descriptive study):

$$N = \frac{Z2pq}{d2}$$

where: q = 1 - p; p is assumed proportion for the study; d is 95% confidence interval is desired with.

d = 0.05. By applying this formula with P = 0.85, N = 195.92 = 196 was obtained. As a result, the required sample size was  $n = 196 \pm 25$ , which is between 171 and

Table 2 Risk and thrombophilia

precipitating factor for VTE:

| Risk and thrombophilia precipitating factors | Frequency (N) | Percentage (%) |
|--|---------------|----------------|
| Underling rheumatology/autoimmunity          |               |                |
| Yes  | 67            | 39.4           |
| Behcet                                       | 2             | 1.2            |
| Gout   | 2             | 1.2            |
| Sjogren                                      | 1             | 0.6            |
| SLE $(\pm APS)$                              | 24            | 14.1           |
| Primary APS                                  | 35            | 20.6           |
| UCTD   | 2             | 1.2            |
| Vasculitis                                   | 1             | 0.6            |
| No   | 103           | 60.6           |
| Provoked at time of presentation             |               |                |
| Yes  | 89            | 52.4           |
| No   | 81            | 47.6           |
| Provoked by                                  |               |                |
| Acquired thrombophilia                       | 78            | 45.9           |
| OCP & hormonal                               | 15            | 8.8            |
| Cancer                                       | 5             | 2.9            |
| Post operation                               | 10            | 5.9            |
| Pregnancy                                    | 23            | 13.5           |
| Prolonged Immobilization & long travelling   | 21            | 12.4           |
| Trauma                                       | 4             | 2.4            |
| Hereditary Thrombophilia                     | 11            | 6.5            |
| Anti thrombin III deficiency                 | 1             | 0.6            |
| Protein C deficiency                         | 2             | 1.2            |
| Protein S deficiency                         | 3             | 1.8            |
| Prothrombin gene mutation                    | 5             | 2.9            |
| No   | 81            | 47.6           |

APS antiphospholipid syndrome, SLE systemic lupus erythematosus, UCTD undifferentiated connective tissue disease, OCP oral contraceptive pill

221. This means that 170 or more measurements/examinations must be performed to have a 98% confidence level that the actual value is within  $\pm 5\%$  of the measured/examined value [16].

# 2.4 Eligibility Criteria

The initial population consisted of n = 5382 patients seen in the hematology clinic during the study period. Adult patients aged 14 years and above (according to hospital policy, the age of majority is 14 years) eligible for treatment at KFMMC, patients diagnosed with thrombosis of any location-venous or arterial, with radiographic examination indicating the presence of thrombosis, as well as patients with completed data, thrombophilia tests and observation history were included in the study. Patients under 14 years old, those ineligibles to be treated in KFMMC, patients without thrombosis, those who were not followed up in the hematology clinic, pediatric age group, patients

without radiographic examination indicating thrombosis, with incomplete data, without thrombophilia tests and without follow-up record were excluded (Fig. 1).

After applying the inclusion and exclusion criteria as shown in Fig. 1, n = 245 cases were flagged as VTE by the informatics system of the clinic. Of these, n = 75 cases were further excluded for the following reasons: they had thrombosis, missing data, no radiographic examination to confirm the diagnosis, no follow-up for either eligibility or transfer to another region. As a result, data of n = 170 patients were included.

## 2.5 Procedures

The study was conducted following ethical approval from the Eastern Province Armed Forces Hospital Institutional Review Board (AFTER-IRB-2024-001, January 28, 2024). Although written informed patient consent was not required for this retrospective study and no patient tissues were used, this study complies with the Declaration of Helsinki.

# 2.6 Data Collection

The entire data set, including laboratory results, patient records, and demographic information, was provided by the health informatics system of KFMMC retrospectively, using ICD-10 codes for thromboembolism. Data included information on age, gender, comorbidities, medications, occupation, and family history of thrombosis (between January 2015 and May 2023). The type (vein, mixed vein, or CNS) and location (lower limb, upper limb, pulmonary, portal, mesenteric, splenic, ovarian vein, orbital, or cardiac) of thrombosis were assessed. Factors that increase risk, such as prolonged bed rest after surgery or travel (immobilization), use of hormones or birth control, exposure to radiation or chemotherapy, history of cancer or autoimmune diseases, and receipt of a COVID-19 vaccine, vaccination after surgery and obesity were also assessed. Finally, the present study compares the epidemiological results of published national data from earlier studies conducted in other provinces of Saudi Arabia (i.e., southern, western and central provinces).

# 2.7 Statistical Analysis

Data entry, cleaning, and coding were done on an Excel worksheet. The data was analyzed using the Social Science Statistical Package (SPSS version 28, Armonk, NY: IBM Corp, USA). The period prevalence rate equation was used to calculate the VTE prevalence rate. The number of new confirmed VTE cases (n = 170) during the study period (January 2015 to May 2023) divided by the total population (n = 5382 patients seen in the hematology clinic) during the same time period × 100, i.e.:

#### **3 Results**

The results of the current study involving n = 170 patients showed that the prevalence of VTE was 3.16%. The mean age of the population was 42.21 (±13.022). Females constituted 70% of the sample, and, thus, the majority of VTE cases were females (Table 1).

Of the included cases, 12.9% smoked e-cigarettes, regular cigarettes or hookah. A positive family history of thrombosis occurs in 13% of cases, and concomitant diseases that may increase the risk of thrombosis occur in 37.6% of cases. The most common comorbidities identified in this cohort were hypertension 18.8% (HTN) and diabetes mellitus 17% (DM); 80.5% of cases were obese or overweight (Table 1).

Table 2 lists thrombophilia (hereditary and acquired) and risk factors for VTE. In 52.4% of cases, VTE was provoked, with the most common triggers of VTE being pregnancy (13.5%) and prolonged immobilization (12.4%). Rheumatological and autoimmune diseases such as Behçet's disease, gout, Sjögren's disease, systemic lupus erythematosus (SLE) with/without antiphospholipid syndrome ( $\pm$  APS), primary antiphospholipid syndrome, vasculitis and unclassified connective tissue disease (UCTD) accounted for a total of 39.4% of cases. The most common rheumatological cause of VTE was primary antiphospholipid syndrome (APS), accounting for 20.6% of cases, followed by systemic lupus erythematosus ( $\pm$  APS), accounting for 14.1% of cases (Table 2).

The lower extremity (56.5%) was the most common site of VTE, followed by the pulmonary vasculature (11.8%) and cerebral vascular accident (CVA) (9.4%). The prevalence of rare sites of thrombosis, such as valvular/cardiac thrombosis, ovarian vein thrombosis, portal vein thrombosis, renal vein thrombosis, splenic or mesenteric vein thrombosis, orbital

| Prevalence rate $(\%) =$ | The # of new diagnosed cases over the period of time $\times 100$ |
|--------------------------|---|
| The value of $(10) =$    | The total population at the same period of time                   |

Given that thrombophilia has both inherited and acquired risk factors for VTE, this study examined both factors using laboratory tests to assess the cause of VTE, known as a thrombophilia test or work up test. To evaluate the association between VTE, site, and body mass index (BMI), a Z-test analysis was applied. The frequency (n) and percentage (%) of categorical variables were used for descriptive statistics. A *p*-value of less than or equal to 0.05 with 95% confidence interval was considered statistically significant.

vein/artery thrombosis and sinus node thrombosis, was as low as 0.6%, reaching 4.7%. In addition, in 58.2% of cases there was only one onset of VTE, and in 28.2% there were two onsets of VTE. The rates of three, four, and five episodes of VTE were 7.6%, 4.1%, and 1.8%, respectively. The highest rate of recurrent VTE was observed in the lower extremities (21.8%), followed by pulmonary artery thrombosis (i.e., pulmonary embolism (PE)) at 10% (Table 3).

Although females have a higher incidence of VTE than men, no statistically significant association was found when

Table 3 Site and frequency of thrombosis

Site and frequency and recurrency of Frequency Percentage thrombosis

| Site                        |    |      |
|-----------------------------|----|------|
| Both mesenteric and splenic | 1  | 0.6  |
| Cardiac thrombosis          | 2  | 1.2  |
| CVA                         | 16 | 9.4  |
| DVT (upper extremities)     | 9  | 5.3  |
| DVT (lower extremities)     | 96 | 56.5 |
| Mesenteric                  | 4  | 2.4  |
| Orbital vein                | 3  | 1.8  |
| Ovarian vein thrombosis     | 1  | 0.6  |
| Portal                      | 5  | 2.9  |
| Pulmonary                   | 20 | 11.8 |
| Renal vein thrombosis       | 1  | 0.6  |
| Sinus thrombosis            | 8  | 4.7  |
| Splenic                     | 2  | 1.2  |
| Valvular/cardiac            | 2  | 1.2  |
| Number of thrombosis        |    |      |
| 1                           | 99 | 58.2 |
| 2                           | 48 | 28.2 |
| 3                           | 13 | 7.6  |
| 4                           | 7  | 4.1  |
| 5                           | 3  | 1.8  |
| Recurrence site             |    |      |
| CVA                         | 8  | 4.7  |
| DVT (upper extremities)     | 1  | 0.6  |
| DVT (lower extremities)     | 37 | 21.8 |
| Mesenteric                  | 2  | 1.2  |
| Portal                      | 2  | 1.2  |
| Pulmonary                   | 17 | 10   |
| Renal                       | 1  | 0.6  |
| Sinus thrombosis            | 2  | 1.2  |
| Splenic                     | 1  | 0.6  |
| No (single site)            | 99 | 58.2 |
|                             |    |      |

examining the association between gender and recurrent thrombosis ( $\chi^2 = 7.23$ , p = 0.61) (Table 4).

# **4** Discussion

This single-center study investigated the prevalence of VTE in a hematology clinic in the Eastern Province of Saudi Arabia between January 2015 and May 2023. During the study period, n = 5382 cases were registered in the hematology clinic of the KFMMC, of which n = 170 people were diagnosed with VTE within the framework of this study from 2015 to 2023, with a prevalence rate of 3.16%. Although the prevalence of VTE in the current cohort is low compared to

Table 4 Correlation between recurrence vs. Gender

| Recurrence                   | Gender    |           | Total     | Chi-square       |
|------------------------------|-----------|-----------|-----------|------------------|
|                              | Female    | Male      |           | <i>p</i> -value  |
| CVA                          | 7 (87.5)  | 1 (12.5)  | 8 (100)   | $\chi^2 = 7.23;$ |
| DVT (upper extremi-<br>ties) | 1 (100)   | 0 (0.0)   | 1 (100)   | p = 0.61         |
| DVT (lower extremi-<br>ties) | 25 (67.6) | 12 (32.4) | 37 (100)  |                  |
| Mesenteric                   | 1 (50)    | 1 (50)    | 2 (100)   |                  |
| Portal                       | 1 (50)    | 1 (50)    | 2 (100)   |                  |
| Pulmonary                    | 10 (58.8) | 7 (41.2)  | 17 (100)  |                  |
| Renal                        | 1 (100)   | 0 (0.0)   | 1 (100)   |                  |
| Sinus thrombosis             | 2 (100)   | 0 (0.0)   | 2 (100)   |                  |
| Splenic                      | 0 (0.0)   | 1 (100)   | 1 (100)   |                  |
| No                           | 71 (71.7) | 28 (28.3) | 99 (100)  |                  |
| Total                        | 119 (70)  | 51 (30)   | 170 (100) |                  |

\*Confidence interval at 95%

other local data, it is important to highlight that these data were limited to an adult hematology clinic, suggesting that the possible actual prevalence of VTE could be higher if minors' data were also included [12, 13]. Further findings of the current study showed a higher prevalence rate than in the United States and European countries, where the prevalence rate of VTE is about 2 per 1000 people [17]. However, these suggestions are the subject of a future multicenter national study that can provide a broad view of the epidemiology of VTE and its characteristics not only in the Eastern Province of Saudi Arabia.

The objective of this study was to investigate the clinical characteristics of VTE and compare them with national data. As shown in Table 5, this allowed to examine differences in epidemiological information between regions of Saudi Arabia, which could facilitate further research on VTE [11, 13, 14, 18].

There are several risk factors for VTE, such as ethnicity, skin color, and other health conditions. Although this study did not compare ethnicity and skin color as risk factors among the Saudi population, previous studies have shown that people with darker skin are more likely to develop VTE than people with brighter skin [19, 20]. In addition, compared with African American and European populations, Asian populations are at lower risk [19, 21–23]. In this study, the majority of VTE cases were in females, which is consistent with some regional studies within Saudi Arabia. Thus, as shown by the studies from Madinah and the Central Province of Saudi Arabia, the female to male ratio was 2:1. On the other hand, in the Southern Province and Jeddah (Western Province) of Saudi Arabia, the ratio was 1:1. Moreover, the results of the current study are inconsistent

| Table 5 A comp  | varison of the cur                      | Table 5         A comparison of the current study with national data | national data                          |   |                                       |  |                                |  |  |   |
|---|---|--|--|---|---------------------------------------|--|--------------------------------|--|--|---|
| Data and Risk<br>factors                                    | Madina study<br>[13]                    | Between<br>Madinah and<br>Eastern Prov-<br>ince^                     | Jeddah study<br>[14]                   | Between Jed-<br>dah and East-<br>ern Province | Southern<br>Province study<br>[18]    | Between<br>Southern<br>Province<br>and Eastern<br>Province | Central Province study<br>[11] | Between Cen-<br>tral Province<br>and Eastern<br>Province | Eastern Prov-<br>ince                    | Between Total<br>of available<br>Provinces and<br>Eastern Prov-<br>ince |
| Total # of<br>patient in the<br>study (N)                   | 385                                     | 0.000*   | 62                                     | 0.000*  | 207                                   | 0.01*  | 1008                           | 0.000*   | 170                                      | 0.000*  |
| Duration of the Jan 2017 to<br>study August 20<br>(4 years) | Jan 2017 to<br>August 2020<br>(4 years) | I  | March 1988<br>to Feb 1992<br>(6 years) | 1   | Jan 2010 to<br>June 2019<br>(9 years) | I  | ten years                      | I  | January 2015<br>to May 2023<br>(9 years) | I   |
| Female/male   | 251<br>(65.2%)/134<br>(34.8%)           | I  | 30 (52%)/ 32<br>(48%)                  | I   | 87 (58%)/120<br>(42%)                 | I  | 738(73.2%)/270(26.8%)          | I  | 119 (70%)/51<br>(30%)                    | I   |
| Smoking   | 22 (5.7%)                               | 0.003*   | 3 (4.5%)                               | 0.08  | NA                                    | NA   | 34 (3.4%)                      | 0.000*   | 22 (12.9%)                               | 0.000*  |
| Obesity   | 25 (6.5%)                               | 0.000*   | 9 (14.5%)                              | 0.000*  | 48 (23%)                              | 0.000*   | 463 (46%)                      | 0.000*   | 137 (80.5%)                              | 0.000*  |
| Family history  | (0.3%) 1                                | 0.000*   | NA                                     | NA  | NA                                    | NA   | 61 (6%)                        | 0.000*   | 23 (13.5%)                               | 0.000*  |
| Recent surgery  | 11 (2.9%)                               | 0.09   | 5 (7%)                                 | 0.55  | 18 (8.7%)                             | 0.30   | 127 (12.5%)                    | $0.01^{*}$   | 10 (5.9%)                                | 0.11  |
| Immobilization<br>including<br>long travel-<br>ling         | 61 (15.8%)                              | 0.28   | 3 (4.5%)                               | 0.10  | 84 (40.6%)                            | 0.000*   | 27 (2.6%)                      | 0.000*   | 21 (12.4%)                               | 0.47  |
| Cancer  | 30 (7.8%)                               | 0.000*   | 6 (9%)                                 | 0.000*  | 31 (15%)                              | 0.000*   | NA                             | NA   | 5 (2.9%)                                 | 0.000*  |
| Trauma or<br>fracture                                       | NA                                      | NA   | NA                                     | NA  | 22 (10.6%)                            | 0.00*  | 27 (2.6%)                      | 0.802  | 4 (2.4%)                                 | 0.28  |
| OCP or<br>hormonal<br>therapy                               | 24 (6.2%)                               | 0.27   | 2 (3.25%)                              | 0.15  | 16 (7.7%)                             | 0.70   | 30 (3.0%)                      | 0.000*   | 15 (8.8%)                                | 0.01*   |
| Pregnancy   | 11 (2.9%)                               | 0.000*   | 6 (9%)                                 | 0.43  | 13 (6.3%)                             | $0.01^{*}$   | 87 (8.6%)                      | $0.04^{*}$   | 23 (13.5%)                               | 0.00*   |
| Hereditary<br>Thrombo-<br>philia cause                      | 11 (2.9%)                               | 0.000  | NA                                     | NA  | NA                                    | NA   | NA                             | NA   | 11 (6.5%)                                | 0.000*  |
| SLE/APA /<br>UCTD   | 4 (1%)                                  | 0.000*   | NA                                     | NA  | 11 (5.3%)                             | 0.01*  | NA                             | NA   | 61 (35.8%)                               | 0.000*  |
| Bechet disease<br>/vasculitis                               | 2 (0.5%)                                | 0.15   | 7 (11%)                                | 0.00*   | NA                                    | NA   | NA                             | NA   | 3 (1.8%)                                 | 0.84  |
| DM  | 28 (7.3%)                               | 0.000*   | NA                                     | NA  | 33 (16.9%)                            | 0.77   | 203 (20.1%)                    | 0.35   | 29 (17%)                                 | 0.85  |
| HTN   | 23 (6.0%)                               | 0.000*   | NA                                     | NA  | NA                                    | NA   | 216 (21.4%)                    | 0.44   | 32 (18.8%)                               | 0.59  |
| CKD or/<br>ESRD   | 9 (2.3%)                                | 0.00*  | NA                                     | NA  | NA                                    | NA   | NA                             | NA   | 13 (7.6%)                                | 0.00*   |
|   |   |  |  |   |                                       |  |                                |  |  |   |

| factors   | [13]            | factors [13] Madinah and [14]<br>Eastern Prov-<br>ince <sup>A</sup> | [14]     | dah and East-<br>ern Province | Province study Southern<br>[18] Province<br>and Easter<br>Province | Southern<br>Province<br>and Eastern<br>Province | Ξ                 | tral Province<br>and Eastern<br>Province | ince                     | of available<br>Provinces and<br>Eastern Prov-<br>ince |
|---|-----------------|---|----------|-------------------------------|--|---|-------------------|--|--------------------------|--|
| Cardiac<br>disease (AF/<br>CHF)                     | 7 (1.9%)        | 0.000*  | 5 (7%)   | 0.65                          | 66 (32%)   | 0.000*  | NA                | NA                                       | 17 (10%)                 | 0.48   |
| Dyslipidemia NA<br>Recurrent VTE 23 (6%)<br>(2nd x) | NA<br>3 23 (6%) | NA<br>0.000*  | NA<br>NA | NA<br>NA                      | NA<br>11 (5.3%)  | NA<br>0.000*                                    | NA<br>246 (24.4%) | NA<br>0.28                               | 27 (15.9%)<br>48 (28.2%) | NA<br>0.001*   |

Table 5 (continued)

with global evidence. Accordingly, it would be erroneous to conclude that females are more likely to develop VTE than males, but it is reasonable to further study this relationship in the future to allow emerging patterns [11, 13, 18, 23]. This may be explained by the fact that the role of gender in the occurrence of first and recurrent VTE is unclear since the use of hormonal therapy and pregnancy may be associated with VTE in females [14, 18, 19, 22]. Hence, association of VTE with gender in Saudi population is the subject for the further research, taking into consideration other reproductive health conditions of females with VTE.

Although smoking is a known risk factor for the development of atherosclerotic disease, there is ongoing debate as to whether it also poses an independent risk the consequences of VTE [25, 26]. The smoking rate (12.9%) in this cohort was high compared with other comparable national data (p=0.000) [11, 13, 14]. Given the differences in genetic and ethnic distribution, compared with conflicting data from both domestic and international sources, this suggests that active smoking is a possible risk factor for VTE in the Eastern Province of Saudi Arabia [26, 27].

Obesity is a recognized risk factor for VTE and its recurrence, regardless of gender [28–31]. According to a study by Hotoleanu et al., obesity increases the risk of VTE by 6.2 times, especially in people aged 50 years and older [32]. Further to this, obesity-associated chronic inflammation and decreased fibrinolysis appear to be two major mechanisms of thrombus formation in obesity [29]. Of n=170 patients in this study, 80.5% were overweight or obese. Further findings from this study support national data that indicate a high prevalence of obesity and overweight as risk factors for VTE. Moreover, this study shows a significantly higher rate (p=0.000) compared to other regional studies in Saudi Arabia [11, 13, 14, 18].

As already mentioned, VTE can be acquired (more often) or hereditary (less often) [1-3, 33]. The results of this study showed that the most common causes were rheumatological and autoimmune diseases (39.4%), pregnancy (13.5%), prolonged immobilization (12.4%), a positive family history of thrombosis (13%), and OCP or hormonal therapy (8.8%). These numbers were significantly higher as compared to regional studies within Saudi Arabia [11, 13, 14, 18]. On the other hand, cancer was more prevalent in Madinah, Jeddah and Southern Province compared to Eastern Province, whereas in Central Province there was no evidence that cancer was a cause of thrombosis (p = 0.000). However, longer hospital stays and VTE as postoperative complications were significantly more common in the Central and Southern provinces compared to the Eastern Province. Further comparable studies in this area are needed to examine the difference in the incidence of postoperative VTE between Eastern Province and Central and Southern provinces. This may indicate that the postoperative approach and in-hospital

VTE incidence is lower than in other regions, with stricter adherence to prophylactic measures to prevent postoperative VTE [18].

The most common and well-known sites of thrombosis in the world are venous thrombosis of the lower extremities and pulmonary embolism (PE). When examining anatomical locations, the distal, femoral, popliteal, and iliac veins have the highest rates of lower extremity thrombosis (40%, 20%, 16%, and 4%, respectively) [34, 35]. Left limb thrombosis is more common than right limb thrombosis when it comes to initial occurrence, but not when thrombosis recurs, despite studies showing that right lower limb thrombosis is superior to left limb thrombosis in patients requiring longer hospital stays and immobilization [36, 37]. In addition, patients with thrombosis of both the right and proximal lower extremity have an increased risk of developing PE [37]. This is caused by increased compression of the internal iliac vessels, stenosis, and blood stasis as a result of immobilization [37]. However, thrombosis in unusual locations (e.g., portal, splenic, mesenteric, orbital, ovarian, and central vasculature) accounts for 10% of cases worldwide. It is also more common in subordinate pathologies such as cancer, inflammatory processes or hereditary consequences [38]. In the current study, the incidence of lower extremity thrombosis was 56.5%, with the majority of cases occurring in the left lower extremity rather than the right lower extremity. This was followed by cerebrovascular accidents (CVA) with 9.4% and pulmonary vascular disorders with 11.8%. These results were consistent with both Saudi and international data [11, 13, 14, 18, 25, 35, 38]. In addition, comparison of data from this study with national data showed that patients in the Eastern Province had a significantly higher rate of recurrent thrombosis [11, 13, 14, 18]. In addition, the incidence of recurrent thrombosis was higher in the left lower extremity (21.8%), which is inconsistent with other studies [36, 37]. However, the study results did not reveal an association between gender and site of recurrent thrombosis (p = 0.61).

Diabetes mellitus, hypertension, and hyperlipidemia represent independent risks of VTE in addition to atherosclerotic cardiovascular changes. Likewise, existing evidence suggests that uncontrolled comorbidities and irregular exercise may increase the risk of VTE [39–41]. In this study, the most common comorbidities were heart disease, chronic kidney disease (CKD), hypertension (HTN), and T2DM, which is consistent with earlier studies in Saudi Arabia. However, compared with Medina's data, the data from this study showed a significantly higher rate of comorbidities (p = 0.000). Regarding recurrent thrombosis, the results of this study conducted in the Eastern Province showed significantly higher rates compared to other regions of Saudi Arabia (p = 0.001). It is important to highlight that the earlier studies in Saudi Arabia did not provide any information on dyslipidemia and VTE for comparison with the data from the current study. Nevertheless, based on the existing evidence and the current research changes in a person's lifestyle and control of blood glucose, blood pressure, cholesterol, triglycerides, and weight loss may reduce the risk of VTE [39, 41, 42].

# 4.1 Limitations

This study has several limitations that are worth considering for future research. The study was a single-center study conducted in a single military hospital with limitations on eligibility criteria. Future studies are expected to be multicenter to provide a more complete picture. The second limitation is that because only cases of VTE in the hematology clinic were recorded, some additional cases of VTE in the hospital may have gone unreported. The third limitation is that because this was a retrospective data collection, some information could not be found or further research could not be conducted. To fully understand the risk of VTE, a larger study involving more centers both domestically and internationally is needed.

# 5 Conclusion

The findings of the current study suggest that the prevalence of VTE in this single-center study in the Eastern Province may have been somewhat underestimated due to the narrow scope of the study and the nature of the hematology clinic, which requires further investigation. Compared with previous studies across Saudi Arabia, significantly higher rates of smoking, obesity, family history, pregnancy, hormone or OCP use, and rheumatological/autoimmune diseases as risk factors for VTE were reported. However, since there are no latest national or global benchmarks for VTE, determining accurate national data is a matter for further multicenter studies across the Kingdom of Saudi Arabia to substantiate findings of the current research. Further to this, additional improvement efforts and a strategic treatment approach are needed to reduce the factors that contribute to VTE in the Eastern Province. Developing an awareness program and supporting lifestyle changes are a critical first step to informing people about VTE and how to reduce its risk.

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### Declarations

**Conflict of interest** The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**Ethical Approval** Approval for the research was obtained from the Armed Force Hospitals Eastern Region Institutional Review Board (IRB), protocol No. AFHER-IRB-2023-022. The study was conducted following ethical approval from the Eastern Province Armed Forces Hospital Institutional Review Board (AFTER-IRB-2024-001, January 28, 2024).

**Consent for Publication** The consent was not required in retrospective study.

**Informed Consent** No informed consent was required for publication of this article.

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