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# Thrombophilia: Demographics and Clinical Presentation in United Arab Emirates

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**Abstract**

**Objectives:** Thrombophilia is a group of disorders that increases the patient's risk of thrombosis. Inherited causes of thrombophilia are challenging to diagnose and once diagnosed may subject the patient to prolonged treatment. The extent of the condition is not well established in UAE and data on prevalence and demographics are lacking. This study aimed at setting a baseline data on the prevalence, demographics and clinical presentation of thrombophilia in UAE.

**Methods:** Retrospective case review study was designed. Data on age, sex, nationality, laboratory results, diagnosis and risk factors were collected.

**Results:** Total of 173 patients was included. The prevalence of inherited thrombophilia in UAE was estimated to be 1 in 200,000 population while acquired thrombophilia was found to be 1 in 15,000 nationals and 1 in 22,000 when considering all nationalities.

**Conclusion:** Diagnosis of thrombophilia requires a panel of investigations based on the clinical presentation and assessment of risk factors. Knowing the prevalence and demographics of the disease can aid the application of proper guidelines in testing and management of patients.

**Keywords**

Thrombophilia, Prevalence, Venous thromboembolism, Protein C, Protein S, Antithrombin, Factor V Leiden

## Introduction

Thrombophilia is defined as increase risk of thrombosis in an individual. It is classified according to the type of risk into hereditary thrombophilia and acquired thrombophilia. Hereditary defects that lead to increased risk of thromboembolism (TE) include defects that increase the procoagulability of the blood, e.g.: APC (acquired activated protein C) resistance, Factor V Leiden, prothrombin mutation, hyperhomocysteinemia and increase factor VIII levels. Venous Thromboembolism (VTE) risks can also increase because of deficiency in natural anticoagulants such as Protein C, Protein S and Antithrombin (AT). VTE is usually the presenting picture but arterial thrombosis can develop in minority of cases. Less usual presentations include visceral or cerebral vein thrombosis, 2nd or 3rd trimester pregnancy loss and severe pre-eclampsia. Tests available for the diagnosis of thrombophilia are sensitive, get affected by many acquired conditions, expensive and time consuming [1,2]. The diagnosis of hereditary thrombophilia also affects patients and might subject them to prolonged anticoagulation therapy.

This study aimed at establishing a baseline data on thrombophilia demographics and clinical features in United Arab Emirates (UAE), since no such data is available for this diverse population. It also addressed a minimal estimate for the prevalence of the disorder. Knowing the actual prevalence and demographics of the disorder in UAE can help in implementing a cost-effective testing methodology targeting selected cases and be used in future for better selection of investigation and treatment protocols.

## Materials and Methods

Case review study was designed to include all subjects (any age and both sexes) who had thrombophilia test done in Al Qassimi Hospital in Sharjah-UAE between the years 2011-2012 (October to September/one year). Age, sex, ethnic group and nationality were collected from patients' registration records. Reason for thrombophilia testing (by physician) and co-existing related risk factors for VTE(smoking, pregnancy, use of oral contraception pills; OCP/hormonal replacement therapy; HRT, varicose veins, age of 50 and older, post-surgery/trauma, prolonged immobilization, other risk factors) [1] were collected from patients' medical records when available. Thrombophilia test results were collected from the laboratory records and final diagnosis was collected from recorded physician's notes. The laboratory performs functional thrombophilia assays, all requests for testing were collected and test results were used to primary identify thrombophilia patients. Other lab investigations including serology for acquired cases as well as patients' medical records (based on thrombophilia test requests) were checked for final confirmation of the diagnosis by the physician. According to the laboratory yearly statistics, an average of 150 patients was estimated to be included in the study. The study was approved by the local Research Ethics Committee (study code number 032013-10) and was conducted in-accordance with the International Conference on Harmonization-Good Clinical Practice (ICH-GCP).

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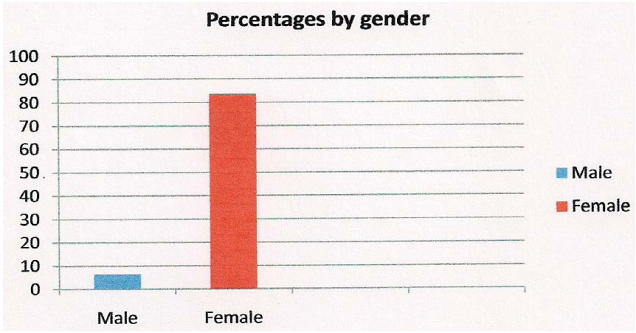


**Figure 1:** Gender distribution among investigated cases

**Table 1:** Nationalities and Ethnic groups of the cases analyzed (N= total number of cases).

| Ethnicity | Number of cases per ethnicity(%*), N=173 | Number of cases per Nationality (%*), N=173 | |
|---|---|---|---|
| Arab | 106 (61%) | UAE | 58 (33.5%) |
| | | Oman | 4 (2.3%) |
| | | Kuwait | 1 (0.6%) |
| | | Bahrain | 1 (0.6%) |
| | | Egypt | 15 (8.7%) |
| | | Syria | 3 (1.7%) |
| | | Jordan | 8 (4.6%) |
| | | Palestine | 5 (2.9%) |
| | | Yemen | 3 (1.7%) |
| | | Tunisia | 1 (0.6%) |
| | | Lebanon | 3 (1.7%) |
| | | Iraq | 4 (2.3%) |
| South Asian | 53 (31%) | India | 19 (11%) |
| | | Pakistan | 20 (11.6%) |
| | | Bangladesh | 5 (2.9%) |
| | | Philippine | 5 (2.9%) |
| | | Afghanistan | 3 (1.7%) |
| | | Serilanka | 1 (0.6%) |
| Persian | 1 (0.6%) | | |
| White | 4 (2.3%) | Cyprus | 1 (0.6%) |
| | | Italy | 1 (0.6%) |
| | | British | 2 (1.2%) |
| African/Black | 8 (4.5%) | Sudan | 5 (2.9%) |
| | | Somalis | 1 (0.6%) |
| | | Cameron | 1 (0.6%) |
| | | Ethiopia | 1 (0.6%) |
| Unknown | 1 (0.6%) | | |

*Percentages may not add to 100 due to rounding to the closer decimal point.

Our hospital covers the thrombophilia testing for 3 out of 7 Emirates with an estimated total population of 1,049,729. UAE nationals account for 18.4% of this population (193,376).

The prevalence of thrombophilia was calculated based on the latest published census from UAE National Statistics Center as:

$$\frac{100 \times (\text{number of thrombophilia cases in Al Qassimi Hospital})}{(\text{Estimated total population in the catchment areas for the selected hospital site})}$$

The rest of the data (e.g. demographics and clinical features) were reported in a descriptive manner or as percentages/ frequencies (where applicable). Missing data were reported separately for each variable as 'unknown'.

## Results and Discussion

Total of 173 patients were included in the analysis. Nine (5%) were from the pediatrics age group and 164 (95%) were adults (age ≥ 18 years). The majority of the investigated population for thrombophilia were females (83.8% of the cases), as shown in Figure 1.

Ethnicities and nationalities of the patients are shown in Table 1. UAE nationals were consisting around 34% of the cases.

**Table 2:** Inherited and acquired thrombophilia final diagnosis

| Diagnosis | | Documented Diagnosis (%*), N=173 | Lab confirmed Diagnosis |
|---|---|---|---|
| Inherited Thrombophilia | Protein C Deficiency | 1 (0.6%) | 0 |
| | Protein S Deficiency | 1 (0.6%) | 0 |
| | Antithrombin Deficiency | 0 | 1 (0.6%) |
| | Factor V Leiden | 1 (0.6%) | 0 |
| | Thrombophilia, not specified | 2 (1.2%) | 0 |
| Acquired Thrombophilia | SLE (Systemic Lupus Erythematosus) | 17 (9.8%) | 9 (5.2%) |
| | APL (Antiphospholipid antibodies) | 3 (1.7%) | 3 (1.7%) |
| | Autoimmune, not specified | 22 (12.7%) | |
| | Thrombosis secondary to infection | 1 (0.6%) | |
| | Malignancy related thrombosis | 2 (1.2%) | |
| | Hypervescosity syndromes | 1 (0.6%) | |
| | Post-surgical thrombosis | 1 (0.6%) | |
| | Thrombosis secondary to asphyxia | 1 (0.6%) | |
| No diagnosis made | | 119 (68.8%) | |

*Percentages may not add to 100 due to rounding to the closer decimal point.

**Table 3:** Risk factors for thrombosis predisposition

| Risk Factor | Number of cases (%), (N=173) | Risk Factor | Number of cases (%), (N=173) |
|---|---|---|---|
| Age (≥ 50yr) | 10 (5.8%) | Hypothyroidism | 2 (1.2%) |
| Surgery | 5 (2.9%) | Atherosclerosis | 1 (0.6%) |
| Trauma | 2 (1.2%) | Varicose veins | 1 (0.6%) |
| Liver disease | 2 (1.2%) | Infection | 1 (0.6%) |
| Congenital heart disease | 1 (0.6%) | Intrauterine hypoxia | 1 (0.6%) |
| Obesity | 10 (5.8%) | Positive family history | 2 (1.2%) |
| Smoking | 7 (4%) | Positive previous history of VTE | 3 (1.7%) |
| Pregnancy | 57 (33%) | Combination of 2 risk factors | 17 (9.8%) |
| Post-partum | 2 (1.2%) | Combination of 3 risk factors | 2 (1.2%) |
| OCP/HRT | 3 (1.7.%) | No risk factors | 30 (17%) |
| Malignancy | 2 (1.2%) | Unknown (not documented) | 42 (24%) |

Prevalence of inherited thrombophilia based on documented diagnosis was found to be 1 in 200,000 populations and this didn't differ between total population and among UAE nationals only. The prevalence of acquired thrombophilia was 1 in 22,000 populations when the total population was considered but acquired thrombophilia was more common among UAE nationals with a prevalence of 1 in 15,000 national (Table 2).

United Arab Emirates consists of 7 major cities (Emirates) with a total population of 4,106,427 (as per latest published census). The hospital where the study was conducted covers all thrombophilia investigations for 3 of these major cities. As mentioned before, the estimated population in the hospital's catchment area is 1,049,729. The prevalence estimated here may not reflect the entire country but it gives a preliminary idea about the extent of the disorder in part of the country which may not differ much from the rest of the remaining four cities.

Risk factor analysis for having VTE showed that 58.7% of cases investigated for thrombophilia were having one or more risk factors for developing thrombosis while 17% were not having any predisposing risk factors. Risk factors were not reported in 24.3% (n=42) of the cases (Table 3).

**Table 4:** Reasons for physicians' referral for testing

| Reason for referral for thrombophilia testing | Number of Cases (%) |
|---|---|
| Recurrent abortion | 63 (36.4%) |
| Brain thrombosis/CVA | 19 (11%) |
| Skin related conditions | 11 (6.4%) |
| IUFD | 14 (8%) |
| Infertility§ | 4 ( 2.3%) |
| Leg pain with or without swelling | 2 (1.2%) |
| DVT | 9 (5.2%) |
| Pulmonary embolism | 3 (1.7%) |
| stillbirth | 3 (1.7%) |
| History of IUGR | 2 (1.2%) |
| Preterm delivery | 4 (2.3%) |
| Other thrombosis* | 7 (4%) |
| Follow up of known cases of thrombophilia | 6 (3.5%) |
| Asymptomatic with positive family history | 1 (0.6%) |
| More than one reason | 24 (13.9%) |
| Unknown (not documented) | 20 (11.6%) |
| Other reasons† | 20 (11.6%) |

§Infertility included 2 with primary infertility and 2 cases with secondary infertility. *Other thrombosis included 3 retinal vein thrombosis, 3 cases of mesenteric thrombosis and 1 case of pelvic thrombosis. † other reasons included joint pain (5), headache (2), neonatal death (2), trauma with brain pathology on CT (2) and 1 case of each of the following: fainting, low platelets count, pancytopenia, neonatal convulsion, neonatal congenital abnormality, ectopic pregnancy, limb weakness, high risk pregnancy and myocardial infarction.

The main reason for the physicians' referral for investigation was a history of recurrent abortion in females (36.4% of the cases). In general, the majority were investigated for gynecological and obstetrics reasons (52% of the patients) followed by admissions for cerebrovascular accidents including CNS thrombosis (11%). Combination of more than one indication for performing the test was seen in 13.9% of the cases. The reason for testing was not documented in 11.6% of the cases. Table 4 summarizes the main causes of testing.

Positive previous thrombotic history was confirmed in 16 cases (9%). All documented cases with the diagnosis of hereditary thrombophilia had predisposing risk factors; some had positive previous history of thrombosis as well. One case of protein C deficiency had varicose veins as risk factor and was investigated for presenting with deep vein thrombosis (DVT). The patient who was diagnosed with protein S deficiency had past history of recurrent DVTs and presented with mesenteric and pelvic vein thrombosis. In this patient, smoking was documented as a risk factor. A third case with confirmed factor V Leiden was a pregnant lady. Two cases were diagnosed as thrombophilia not specified; one of them had history of recurrent abortions. Specific testing for hereditary thrombophilia was requested in 39 cases (22.5%), one case of which had a positive family history of hereditary thrombophilia. The test was negative in this case. Fourteen other cases were investigated for hereditary causes due to positive past history of thrombosis, four of which has recurrent (more than 1) thrombotic event. Tests for acquired causes were requested in 37 cases while 97 cases were screened for both causes (56% of the cases).

## Conclusion

Inherited thrombophilia is a genetically determined group of disorders that increase the patient's risk of venous thrombosis or thromboembolism [3-5]. Some of these disorders are more common than others. This study aimed at establishing a baseline data on demographics, causes and clinical features of the disorder and giving a suggestive estimate of the prevalence (at least in part of the country). The prevalence of inherited thrombophilia is reported to be variable and it is frequently reported according to the specific defect. The prevalence of Factor V Leiden in normal Caucasians found to be 3-7%, Prothrombin mutation 1-3%, Antithrombin deficiency 0.02-0.04%, Protein C deficiency 0.2-0.5% and Protein S deficiency 0.1-1% [5-9]. In one study from Kingdom of Saudi Arabia, protein S deficiency was reported to be more frequent than Protein C and Factor V Leiden [7]. A single study on prevalence of VTE in UAE was conducted by Al Sayegh et al. [10] without reporting details on the predisposing hereditary factors. From here comes the need to conduct this study. In our series of cases, the prevalence was less than reported internationally. Protein C deficiency, Protein S deficiency and Factor V Leiden were found to be 0.00095% in total UAE population. This lower frequency might be attributed to the limited number of facilities that offer special thrombophilia testing; samples collected from far places can travel up to one hour to reach the reference lab. Inappropriate transportation conditions can affect the final laboratory results, hence, the diagnosis. Acquired thrombophilia found to be more common than inherited. Being unable to access data on the number of cases in other parts of UAE sat a limitation on estimating the exact prevalence for the whole country. Preliminary estimates from this study can be further expanded in larger scale studies to cover the prevalence in the other Emirates. The study also reported discrepancy between recorded number of thrombophilia patients diagnosed by physicians and the actual number of cases confirmed by the panel of tests in our lab (which was less than physician documentation). This is explained partially by the preference of some patients to perform the test in other laboratories due to cost issues and getting the results to their physicians. Another reason might be the lack of knowledge among some physicians on the medical conditions that give false positive results and the need of at least two positive results, 3-6 months apart in-order to confirm the diagnosis of heritable thrombophilia. This has led to the over estimation of the condition by physicians. Many acquired causes can also predispose to VTE and might interfere with the diagnosis of inherited thrombophilia [3].

Efforts were made to minimize bias. All cases tested for thrombophilia during the study period were included to minimize selection bias. Details of data on risk factors were collected in all accessible patients' records.

Patients with inherited thrombophilia can present with unprovoked VTE, recurrent thrombotic events, thrombosis in young age (<50) and positive family history of thrombosis [11]. If a female, then she might have a history of unexplained fetal losses in the first trimester. Some cases present with more severe cerebral or visceral thrombosis [3,12,13]. Skin necrosis can develop in patients with inherited thrombophilia when treatment with vitamin K antagonist is initiated. Diagnosis of inherited thrombophilia depends on a panel of investigations to specify and confirm the present defect. This requires the appropriate laboratory tests and the suggestive clinical history to be present in order to reach to the correct diagnosis. Once the diagnosis is confirmed, those patients should be assessed for the need of prophylaxis anticoagulation therapy or prolonged treatment for the acute thrombotic event [14]. Patients with defects such as prothrombin mutations, homozygosity for factor V Leiden, Protein C, Protein S and Antithrombin deficiencies are at higher risk of recurrent VTE [3]. This study provided a baseline demographics and clinical presentation of thrombophilia in UAE population. These data should be confirmed by conducting larger scale studies with participation from different parts of the country for better understanding of the disease and the interactions with risk factors. The current published data can be used to establish investigation and diagnostic protocols in order to make it more cost-effective.

## Conflict of Interest/Financial Disclosure

The authors declare that they have no conflict of interest relevant to the study submitted to the journal for review and publication. They have no affiliation with or financial involvement in any organization or entity with a direct financial interest in the subject matter or materials discussed in this study. The study was personally funded by the primary investigator.

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