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ORIGINAL RESEARCH article

Inherited thrombophilia and risk factor interactions in a multigenerational Libyan family with deep vein thrombosis

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Keywords: Coagulation factors, deep vein thrombosis, Libya, risk factors

Abstract: Deep vein thrombosis (DVT) is a major vascular disorder with significant morbidity and mortality. Inherited thrombophilia defects and acquired risk factors both contribute to its pathogenesis. Familial clustering suggests a strong genetic component, but data from Libyan families are limited. This study aimed to investigate inherited and acquired risk factors for DVT in a multigenerational Libyan family with a history of venous thrombosis. We recruited 10 family members: four symptomatic individuals, three asymptomatic individuals, and three controls. The index case had heterozygous factor V Leiden. We analyzed blood samples collected between October 2024 and January 2025 for fibrinogen, factor V, factor VIII, protein C, protein S, D-dimer, and complete blood count parameters. Body mass index and smoking status were also recorded. Factor V deficiency and elevated factor VIII were each observed in 6/10 participants. Elevated factor VIII was present in all four symptomatic patients. Fibrinogen was elevated in 2/10 participants, both asymptomatic. Protein C deficiency was found in 2/10 participants, and Protein S deficiency in; all were symptomatic. D-dimer was elevated in only one symptomatic patient. Obesity was present in 8/10 participants, and smoking in 3/10, all of whom were symptomatic males. However, between-group comparisons did not reach the significance level. These preliminary findings suggest that inherited thrombophilia factors, particularly factor V deficiency and elevated factor VIII, may contribute to DVT susceptibility in this family, with modifiable risk factors possibly acting as triggers.

Introduction

Deep vein thrombosis (DVT) represents a significant vascular disorder characterized by the pathological formation of blood clots within the deep venous system, most commonly affecting the lower extremities. This condition, together with its potentially fatal complication of pulmonary embolism, constitutes a major global health burden, accounting for substantial morbidity and mortality worldwide. The intricate balance between procoagulant and anticoagulant forces within the circulatory system is essential for maintaining normal hemostasis while preventing pathological thrombosis. When this equilibrium is disrupted-whether through genetic mutations, acquired conditions, or environmental factors-individuals become susceptible to the development of venous thromboembolism (VTE) [1, 2]. The coagulation cascade, a complex series of enzymatic

reactions, plays a pivotal role in hemostasis through intrinsic and extrinsic pathways that converge to form the common pathway. This sophisticated system involves numerous clotting factors, including factor V, factor VIII, fibrinogen, and the natural anticoagulants protein C and protein S, all of which work in concert to regulate clot formation and dissolution [3, 4]. Disruptions in any of these components can predispose individuals to either bleeding disorders or thrombotic conditions [5]. The physiological importance of this regulatory pathway is demonstrated by the occurrence of hereditary thrombophilia in individuals with genetic defects that affect the sensitivity of coagulation factors to inactivation by activated protein C (APC) or alter the levels of natural anticoagulants [6].

Genetic predisposition plays an increasingly recognized role in the pathogenesis of DVT, with several heritable risk factors having been identified. Among the most significant are deficiencies in protein C and protein S, which serve as crucial natural anticoagulants that inactivate factors Va and VIIIa, thereby regulating the coagulation cascade [7]. Protein C deficiency, either inherited or acquired, affects approximately 1 in 200 to 500 individuals in the general population and is associated with a significantly increased risk of venous thromboembolism [8]. Similarly, protein S deficiency, which may be quantitative or qualitative in nature, impairs the body's ability to regulate coagulation and predisposes individuals to thrombotic events [9]. The factor V Leiden mutation, characterized by resistance to APC-mediated inactivation, represents the most common genetic cause of hereditary thrombophilia, particularly prevalent among individuals of European descent [10, 11]. Elevated levels of procoagulant factors, particularly Factor VIII and fibrinogen, have also emerged as independent risk factors for VTE. Factor VIII, a crucial cofactor in the tenase complex, accelerates the activation of factor X, leading to enhanced thrombin generation and fibrin formation [12]. High factor VIII levels may increase the rate of thrombin and fibrin formation, potentially contributing to a hypercoagulable state [13]. Fibrinogen, in addition to serving as the substrate for fibrin formation, plays a major role in platelet aggregation and plasma viscosity, with elevated levels commonly observed in inflammatory and prothrombotic states [14]. Beyond genetic factors, numerous clinical and environmental risk factors contribute to DVT development. Obesity, now recognized as a global epidemic, exerts significant prothrombotic effects through chronic inflammation, impaired fibrinolysis, and alterations in coagulation factor levels [15-17]. The relationship between obesity and thrombosis is well-established, with elevated body mass index (BMI) correlating with increased fibrinogen levels and enhanced thrombotic risk [18].

Smoking, another modifiable risk factor, promotes thrombosis through vascular damage, increased concentration of clotting factors, and alterations in vessel wall properties [19]. Hypertension and diabetes mellitus, while traditionally associated with arterial disease, have also been implicated in venous thrombotic risk [16, 20, 21]. Additional risk factors include older age, pregnancy, estrogen-containing medications, malignancy, surgery, trauma, and prolonged immobilization [22, 23]. The clinical diagnosis of DVT relies on a combination of physical examination findings, including tenderness, warmth, erythema, edema, and specific signs such as Homan's sign [24], along with objective diagnostic testing. Biomarkers play an increasingly important role in diagnosis and risk stratification. D-dimer, a fibrin degradation product, is widely used in clinical practice to exclude the diagnosis of DVT, while elevated levels may indicate ongoing thrombotic activity [1]. Other biomarkers, including P-selectin, microparticles, and inflammatory cytokines, provide additional insights into the pathophysiology of venous thrombosis and may help identify individuals at increased risk [25].

Venous thromboembolism represents a substantial public health concern, ranking as the third leading cause of cardiovascular death in the United States, with an estimated annual incidence of more than 900,000 cases [26]. In Europe, similar figures demonstrate the significant impact of VTE, with more than 465,000 cases of DVT and 295,000 cases of PE occurring annually, resulting in more than 370,000 VTE-related deaths [25]. Despite

advances in prevention and treatment, VTE continues to pose a major challenge to healthcare systems worldwide. Familial clustering of DVT suggests a strong genetic component in the pathogenesis of venous thrombosis. The identification of heritable thrombophilic defects within affected families enables targeted screening and preventive strategies for at-risk individuals. However, the interplay between genetic predisposition and environmental factors remains complex, and the precise contribution of various risk factors may vary across different populations. Ethnic and geographic variations in the prevalence of thrombophilia defects underscore the importance of population-specific studies to guide clinical practice [23]. The present study aims to investigate the relationship between genetic risk factors and the development of DVT within a multigenerational Libyan family with a history of venous thrombosis. By examining biochemical markers, including coagulation factors (fibrinogen, factor V, factor VIII, protein C, and protein S), D-dimer levels, and complete blood count parameters, this research seeks to elucidate the contribution of inherited thrombophilia to DVT pathogenesis in this family. Furthermore, the study explores the interaction between genetic predisposition and modifiable risk factors such as obesity and smoking, providing insights into the complex interplay between hereditary and environmental influences on thrombotic risk. The findings of this investigation may have important implications for early detection, risk stratification, and preventive strategies in genetically predisposed populations, ultimately contributing to improved outcomes for individuals at risk of VTE.

Materials and methods

Participants: The present study was conducted on a multigenerational Libyan family with a history of DVT. A total of 10 participants were selected, including the index case (G2M END ″42y″) with heterozygous factor V Leiden (R506Q) mutation as indicated by green circles in the pedigree (**Figure 1**). The cohort included four symptomatic individuals, three asymptomatic individuals, and three controls. The participants span several generations of the family: G_1ST, G_2ND, G_2RD, G_2END, and G_3RD. There is no G_4TH generation. The distribution across the pedigree is as follows: G_1ST: three individuals (two controls, one asymptomatic), G_2ND: two individuals (one symptomatic, one control), G_2END: four individuals (three symptomatic, one asymptomatic), and G_3RD: one individual (asymptomatic).

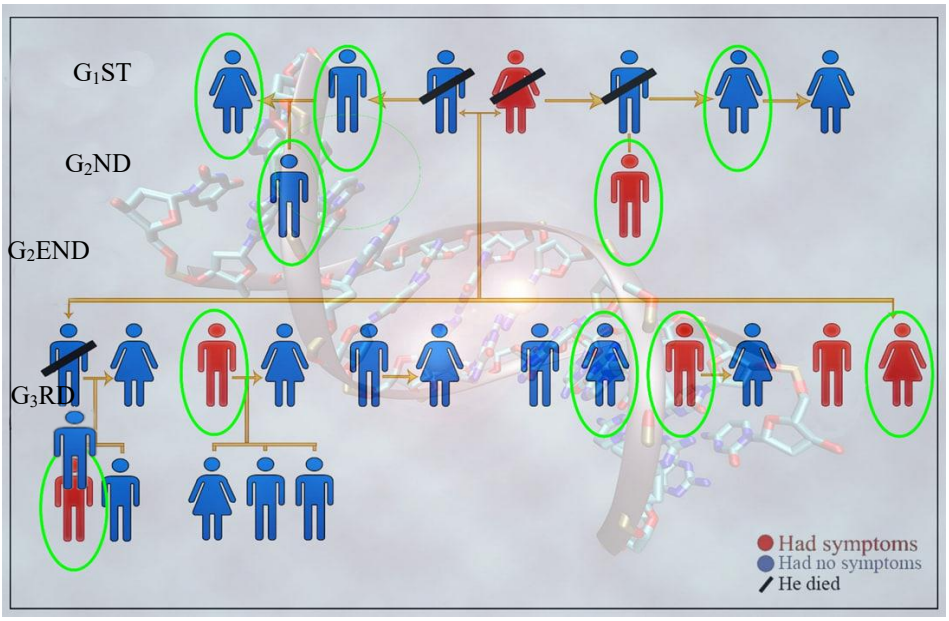


Figure 1: Pedigree of the studied Libyan family showing the selected participants (circled) across three generations, with affected asymptomatic and control individuals indicated

The symptomatic individuals were diagnosed at the emergency unit of vascular surgery with venous thrombosis in the legs [3]. The age range of all participants was between 17 and 68 years. The control individuals were relatives from the same family with no history of DVT. Samples were collected between October 2024 and January 2025 from Sirte City, North Libya. For all participants, information regarding DVT risk factors, including obesity, smoking, and BMI, was recorded. The mean ages for the asymptomatic, symptomatic, and control groups are presented in **Table 1**. All the participants were informed about the study, and written consent from each volunteer was obtained prior to blood sampling. A written questionnaire was given to each volunteer. The questionnaire included questions about age, sex, smoking, and other chronic diseases.

Sample collection: A total of 6.0 mL of whole blood was collected at the venipuncture site from each participant and distributed into three distinct tubes. For complete blood count (CBC) analysis, an EDTA test tube was used and immediately analyzed. Furthermore, anticoagulant test tubes with sodium citrate were employed for the blood clotting factor levels (protein S+C, FV, FVIII, fibrinogen) and D-dimer. Specimens were promptly dispatched to Al-Shark Laboratories for medical analysis following acquisition.

Table 1: Mean age in each group under study

Parameter	Asymptomatic (n=3)	Symptomatic (n=4)	Control (n=3)
Age (years)	42.67±25.50	43.25±6.85	48.67±20.03

Blood clotting factor reagents: Factor deficient buffer (factor V analysis), Buffer for factor VIII, factor deficient buffer for Fibrinogen (Bio-Fibrin), protein S and C innovance free PS AG Buffer (protein S and C analysis), Bromochromate protein C reagent (protein C analysis), innovance free protein S reagent (protein S analysis), and fibrinogen H_2O reagent (Fibrinogen analysis).

Complete blood counts analysis: Standard hematology reagents as per manufacturer's protocols and *D-dimer analysis:* D-dimer Gen. 2 Calibrator Set and D-dimer Gen. 2 Control I/II.

Instruments and equipment: The following instruments were used for biochemical and hematological analyses: *Integra 400 Plus (Roche):* A fully automated clinical chemistry analyzer used for D-dimer biomarker analysis. *Sysmex CS-2400:* An automated coagulation analyzer used to assess blood clotting parameters. *Sysmex XN-550:* A compact, fully automated hematology analyzer designed for CBC and five-part white blood cell differentials.

Ethical approval: The study was approved by the Ethics Committee for Medical Research (reference number 019-MJ-04-2026).

Statistical analysis: All statistical analyses were performed using IBM SPSS Version 21 (SPSS Inc., Chicago, IL, USA). Descriptive analyses were calculated: Mean, standard deviation, and percentage. Comparative analysis between groups (asymptomatic, symptomatic, and control) was conducted using the Mann-Whitney *U* test for non-parametric data. Differences were considered significant at $p<0.05$.

Results

This study included ten volunteer participants from a single Libyan family with a documented history of DVT. Based on the pedigree, participants belonged to Generations I-III; there was no Generation IV. Generation I included four individuals, Generation II included five individuals, and Generation III included one individual. The cohort was stratified into four symptomatic individuals, three asymptomatic individuals, and three controls.

Participants ranged in age from 17 to 68 years. Based on the subject codes, there were four females and six males (**Table 2**). Blood samples were collected between October 2024 and January 2025 in Sirte City, North Libya. The current study includes 10 relatives from both sides of the family who are genetically affected (**Figure 1**). For more details, volunteers' full information on diseases, diagnostics, treatments, and their chronic diseases (hypertension and diabetes mellitus) is in **Table 3**, and risk factors such as body mass index and smoking are shown in **Table 4**.

Table 2: Demographic characteristics of the study participants

Subject code	Generation	Gender	Age (years)	Clinical group
G_{1M} ST	I	Male	64	Control
G_{1F}ST	I	Female	56	
G_{2M}ND	II	Male	26	
G_{1F} ST	I	Female	68	asymptomatic
G_{2F} END	II	Female	43	
G_{3M}RD	III	Male	17	
G_{1M}ND	I	Male	41	symptomatic
G_{2M}END	II	Male	42	
G_{2ME}ND	II	Male	55	
G_{2F}END	II	Female	37	

Note: G = Generation, F = Female, M = Male

Table 3: Volunteers' full information

	Subject Code	Gender	Age (y)	Diagnosis of DVT	Treatment of DVT	other diagnosis disease (Year)	Medicine
CONTROL	G_{1M} ST	Male	64	No	No	hypertension BPH in 2009	divan12 /80 omnoc 0.4-5
	G_{1F}ST	female	56	No	No	D.M (2014)	diamicron 90, mellitofix 12.5/500 aspirin 75 simvastatin 40
	G_{2M}ND	male	26	No	No	None	None
ASYMPTOMES	G_{1F} ST	female	68	No	No	none	None
	G_{2F} END	female	43	No	No	none	None
	G_{3M}RD	male	17	No	No	None	None
SYMPTOMES	G_{1M}ED	male	41	yes	2017 Apixaban 5.0 mg	depression (2022)	zyprexa 5
	G_{2M} END	male	42	yes	2021 xerelto 20 mg	none	None
	G_{2M}ND	Male	55	yes	2009 Apixaban 5.0 mg	BPH (2022)	flopadex 8
	G_{2F}END	female	37	yes	2022 (Xerelto 10 mg	None	None

BMI: body mass index, D.M: diabetes mellitus, HTN: hypertension
G_{1F}ST: Female first generation, G_{1M}ST: Male first generation

Risk factors analysis: In **Table 4**, among the 10 participants, obesity (BMI>30 kg/m²) was present in 8/10. No participant was overweight (BMI 25-29.9), and 2/10 had a normal BMI. Smoking was reported by 3/10, all of whom were symptomatic males. Hypertension was present in 1/10, and diabetes mellitus was present in 1/10.

Table 4: Risk factors and clinical characteristics of the participants

	Subject Code	Age	BMI (kg/m²)	Smoking	Hypertension	Diabetes mellitus
Control	G_{1M} ST	64	42.3	No	No	Yes
	G_{1F}ST	56	33.48	No	Yes	No
	G_{2M}ND	26	24.9	No	No	No
Asymptomati	G_{1F} ST	68	36.21	No	No	No
	G_{2F} END	43	37.45	No	No	No
	G_{3M}RD	17	23.11	No	No	No
symptomatic	G_{1M}ED	41	47.27	Yes	No	No
	G_{2M} END	42	38.76	Yes	No	No
	G_{2M}ND	55	32.5	Yes	No	No
	G_{2F}END	37	36.1	No	No	No

Coagulation factors analysis: Coagulation data were available for all 10 participants (**Table 5**). Fibrinogen was elevated above 400 mg/dL in 2/10 participants; both were asymptomatic (G1F ST68=480 mg/dL; G2F END43= 435 mg/dL). One additional asymptomatic subject (G3M RD17) had a borderline normal value (391 mg/dL). No symptomatic patient or control had elevated fibrinogen. Factor V was decreased below 0.91 in 6/10 participants: all three asymptomatic subjects (G1F ST68=0.51; G2F END43=0.52; G3M RD17=0.53), two symptomatic patients (G2M END42=0.41; G2M ND55=0.55), and one control (G1F ST56=0.89). The symptomatic values of 0.97 in G1M ST41 and 1.065 in G2F END37 were within the normal range. Factor VIII was elevated above 150% in 6/10 participants: all four symptomatic patients (G1M ST41=200%; G2M END42=155%; G2M ND55=213%; G2F END37=217%), and two controls (G1M ST64=300%; G1F ST56=306%). Asymptomatic subjects had normal factor VIII levels. Protein C was decreased below 70% in 2/10 participants, both symptomatic: G1M ST41=66% and G2M ND55= 63%. Protein S was decreased in 1/10 participants: the symptomatic patient, G1M ST41=66%. All other participants had normal Protein S levels. D-dimer was elevated above the normal range in 1/10 participants: the symptomatic patient, G2M END42=1.66 µg/mL. All other participants had normal D-dimer levels. Although descriptive differences were observed in the mean levels of coagulation factors across the three groups, these differences were not significant.

Complete blood count analysis: RBC counts were below the normal range in 2/4 symptomatic patients: G_{2M}ND (55 y)=4.25 million/mcL and G_{2F} END (37 y)=4.49 million/mcL. WBC was elevated in one control participant, G1M ST64=11.4 $\times 10^3/\mu L$; all other WBC values were within the normal range. Lymphocyte percentages were abnormal in one participant: control G1F ST (56 y) = 46.3% (elevated). Neutrophil percentages were elevated in three participants: control G2MND (26 y) = 68.0%, symptomatic G2M END (42 y)=63.5%, and symptomatic G2F END (37 y)=63.0%. Similarly, the mean values for all complete blood count parameters were broadly similar across groups, with no significant differences observed.

Table 5: Coagulation factor levels of the participants

	Subject code	Age years	Fibrinogen (mg/dL)	Factor V	Factor VIII (%)	D-dimer (µg/mL)	Protein S (%)	Protein C (%)
Control	G_{1M} ST	64	351	1.01	300 ↑	0.36	86.0%	78.0%
	G_{1F}ST	56	227.6	0.89 ↓	306 ↑	0.38	95.8	133.1
	G_{2M}ND	26	265	1.12	135	0.21	104%	95.0%
	Mean± SD		281.20± 63.28	1.007± 0.115	247.00± 97.04	0.317± 0.093	95.27± 9.01	102.03± 28.22
Asymptomatic	G_{1F} ST	68	480 ↑	0.51 ↓	108	0.37	94.0%	88.0%
	G_{2F} END	43	435 ↑	0.52 ↓	124	0.38	102	86.0%
	G_{3M}RD	17	391	0.53 ↓	141	0.39	111%	84.0%
	Mean± SD		435.33± 44.50	0.520± 0.010	124.33± 16.50	0.380± 0.010	102.33± 8.51	86.00± 2.00
Symptomatic	G_{1M}ED	41	355	0.97	200 ↑	0.31	66 ↓	66 ↓
	G_{2M} END	42	391	0.41 ↓	155 ↑	1.66 ↑	116%	106%
	G_{2M}ND	55	366	0.55 ↓	213 ↑	0.25	83.0%	63.0%↓
	G_{2F}END	37	305	1.065	217 ↑	0.285	95.0%	86.0%
	Mean ± SD		354.25± 36.12	0.749± 0.318	196.25± 28.44	0.625± 0.690	90.00± 21.02	80.25± 19.97
Normal range			150-400	0.91-1.19	70-150	0.0-0.5	72-131.4% (M) 64.-115.3% (F)	70-140%

↑ = elevated above normal range; ↓ = decreased below normal range; N/A = data not available

Table 6: Complete blood count parameters of the study participants

Group	Subject Code	Age years	WBC (x10³/µL)	RBC (million/mcL)	Lymphocytes (%)	Neutrophils (%)
Control	G_{1M} ST	64	11.4	5.39	29	59
	G_{1F}ST	56	8.87	4.64	46.3 ↑	43.1
	G_{2M}ND	26	9.7	5.29	23	68 ↑
	Mean±SD		9.99±1.29	5.107±0.407	32.77±12.10	56.70±12.61
Asymptomatic	G_{1F} ST	68	7.3	5.25	29	62
	G_{2F} END	43	9.0	5.1	31	58.5
	G_{3M}RD	17	10.7	4.95	33	55
	Mean±SD		9.00±1.70	5.110±0.151	25.67±9.45	58.50±3.50
Symptomatic	G_{2M}ND	55	6.5	4.25↓	29	57
	G_{2M} END	42	10.55	5.34	26	63.5 ↑
	G_{1M}ST	41	8.3	4.81	28	55
	G_{2F}END	37	8.8	4.49 ↓	27	63 ↑
	Mean±SD		8.54±1.67	4.723±0.471	27.50±1.29	59.63±4.27
Normal range			4-11	4.5-5.9	22-33	54-62

↓ = decreased below normal range; ↑ = elevated above normal range; N/A = data not available

Table 5 summarizes the overall abnormal findings in this study (coagulation factor levels among the participants).

Table 5: Summary of abnormal coagulation factor levels among the participants

Biomarker	Abnormal/available	Asymptomatic	Symptomatic	Control
Fibrinogen (↑)	2/10 (20.0%)	2 (66.7%)	0 (00.0%)	0 (00.0%)
Factor V (↓)	6/10 (60.0%)	3 (100%)	2 (50.0%)	1 (33.3%)
Factor VIII (↑)	6/10 (60.0%)	0 (00.0%)	4 (100%)	2 (66.7%)
protein C (↓)	2/10 (20.0%)	0 (00.0%)	2 (50.0%)	0 (00.0%)
Protein S (↓)	1/10 (10.0%)	0 (00.0%)	1 (25.0%)	0 (00.0%)
D-dimer (↑)	1/10 (10.0%)	0 (00.0%)	1 (25.0%)	0 (00.0%)

Discussion

Factor V Leiden is the most common inherited genetic cause of thrombophilia (an increased tendency to form abnormal blood clots). Caused by a single point mutation (a transition of guanine to adenine at nucleotide 1691) in exon 10 of the F5 gene. This mutation replaces the amino acid arginine with glutamine at position 506 (Arg506Gln) in the factor V protein. It is inherited in an autosomal dominant manner [24]. Studies suggest that inherited thrombophilia factors may contribute to DVT susceptibility within this Libyan family. Coagulation abnormalities were observed across three generations; however, the small pedigree and incomplete laboratory data preclude definitive conclusions about the mode of inheritance. Factor V deficiency and elevated factor VIII were the most frequently observed abnormalities, each present in 6/10 participants. Factor V deficiency was noted in all three asymptomatic subjects, two of four symptomatic patients, and one control. Although this is broadly consistent with prior reports linking factor V abnormalities to hereditary thrombophilia [6], the observed reductions could reflect analytical variation, consumptive processes, or anticoagulant effects, and should therefore be interpreted cautiously.

Elevated factor VIII was present in all four symptomatic patients and in two control participants (G1M ST64=300%; G1F ST56=306%). The persistence of elevated factor VIII in treated symptomatic patients raises the possibility of a sustained hypercoagulable state, consistent with prior observations that high factor VIII may act as an independent risk factor for venous thrombosis [13]; however, factor VIII is an acute-phase reactant and may be influenced by inflammation, stress, and treatment, so these findings should be considered hypothesis-generating rather than conclusive. Fibrinogen was elevated in 2/10 participants, both asymptomatic, with one additional asymptomatic subject showing a borderline value (391 mg/dL).

This raises the possibility that fibrinogen could serve as an early marker of hypercoagulability before symptoms appear, consistent with its role in platelet aggregation and plasma viscosity in prothrombotic states [14], but the small number of subjects limits interpretation. Protein C deficiency was observed in 2/10 participants, and protein S deficiency in 1/10; both protein C-deficient cases were symptomatic. D-dimer was elevated in only one symptomatic patient (1/10) and was normal in the remaining participants, suggesting that D-dimer may have limited discriminatory value in this family; however, this may also reflect sampling timing and the chronic rather than acute nature of the hypercoagulable state. The mean coagulation profiles show that factor VIII was highest in controls (247.00±97.04%) and symptomatic patients (196.25±28.44%) but lower in asymptomatic participants (124.33±16.50%). Factor V was lowest in asymptomatic participants (0.520±0.010) and highest in controls (1.007±0.115), while symptomatic patients showed an intermediate mean with wide variability (0.749±0.318). Fibrinogen was highest in asymptomatic.

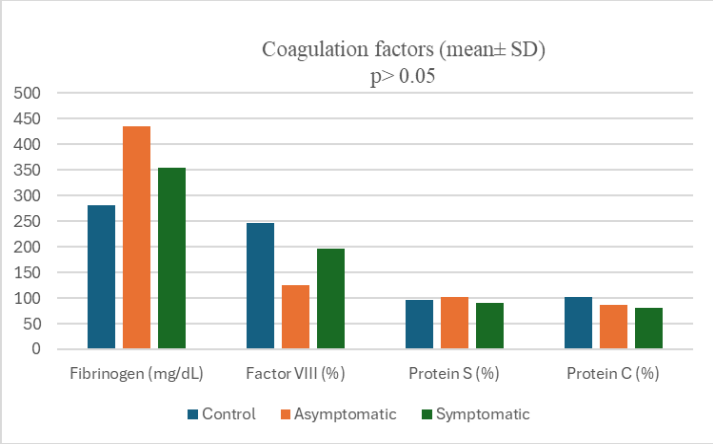


Figure 2: Mean coagulation factor levels (Fibrinogen, factor VIII, protein S, and protein C) among the control, asymptomatic, and symptomatic groups. No significant differences were observed between the groups.

Participants (435.33±44.50) and lowest in controls (281.20±63.28). D-dimer showed a markedly higher and more variable mean in symptomatic patients (0.625±0.690), driven largely by one elevated value. Protein C and protein S means were lowest in symptomatic patients, although the differences were modest and the SD were wide.

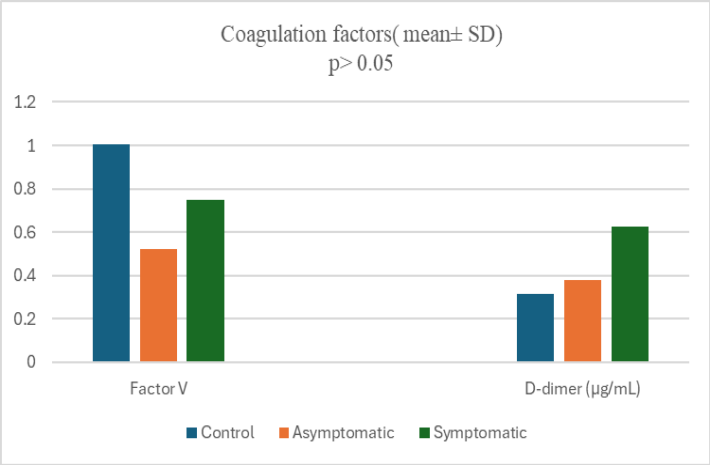


Figure 3: Mean factor V and D-dimer levels among the control, asymptomatic, and symptomatic groups. No significant differences were observed between the groups.

Overall, while these group means suggest possible descriptive differences in coagulation factor profiles, the differences were not statistically significant. The very small group sizes and wide variability mean that these differences should be interpreted cautiously and cannot be considered statistically robust. Obesity was present in 8/10 participants and smoking in 3/10, all of whom were symptomatic males. These Environmental exposures may act as triggers on a background of genetic susceptibility, consistent with the concept that obesity promotes prothrombotic effects through chronic inflammation and impaired fibrinolysis [13]. Hypertension and diabetes mellitus were each present in 1/10 participants. Reduced red blood cell counts were observed in 2/4 symptomatic patients, with sporadic abnormalities in WBC, lymphocyte, and neutrophil counts. These observations raise the possibility that genetic predisposition and environmental factors interact to increase thrombotic risk in this family, but causality cannot be established from this dataset. The high frequency of elevated factor VIII in this family raises the possibility of specific underlying genetic variants; molecular genetic testing would be needed to confirm this. These findings should be considered hypothesis-generating and warrant confirmation in larger, genetically characterized cohorts with complete laboratory data. The mean CBC values were similar across the three groups. WBC counts were slightly higher in controls (9.99±1.29) than in asymptomatic (9.00±1.70) and symptomatic participants (8.54±1.67). RBC means were comparable between controls (5.107±0.407) and asymptomatic participants (5.110±0.151), but lower in symptomatic patients (4.723±0.471), consistent with the reduced RBC counts noted in two symptomatic individuals.

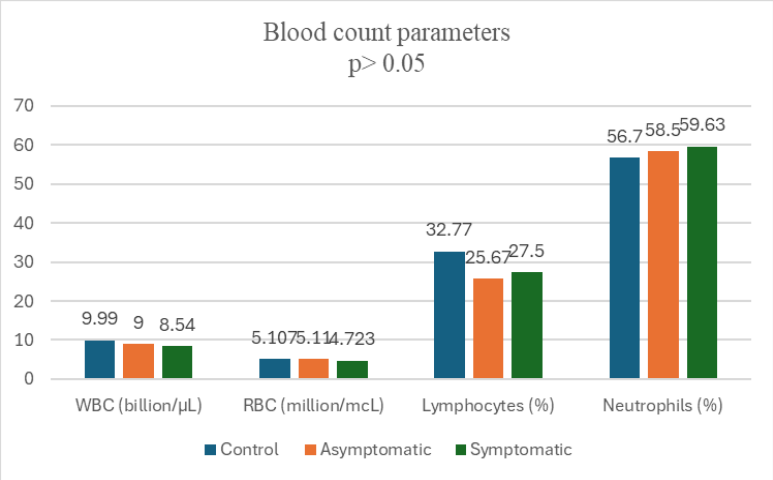


Figure 4: Mean values of white blood cell (WBC), red blood cell (RBC), lymphocyte, and neutrophil counts across the three study groups. No significant differences were observed between the groups.

Lymphocyte and neutrophil percentages showed no consistent group-specific pattern, and the wide standard deviations, particularly for lymphocytes in controls (32.77±12.10%), indicate substantial inter-individual variation. These findings suggest that routine CBC parameters do not show a clear or consistent hematological signature in this family. The lack of statistical significance indicates that any differences are likely to be non-specific and limited by the small sample size. Based on these preliminary observations, further studies are warranted to: (1) perform molecular genetic screening for inherited thrombophilia in all family members at risk, (2) conduct prospective coagulation profiling of at-risk relatives, and (3) evaluate whether lifestyle interventions reduce thrombotic risk in genetically susceptible individuals. Because genetic confirmation was limited to a single index case within a small sample, these findings must be considered preliminary. Comprehensive genetic screening across all at-risk family members, along with larger, genetically characterized population studies, is required to confirm these observations and establish their clinical relevance in the broader Libyan population. However, the small sample size and limited genetic confirmation mean the results are hypothesis-generating and require confirmation in larger, genetically characterized studies.

Conclusion: The study suggests that inherited thrombophilia factors may contribute to DVT susceptibility within this Libyan family. Elevated factor VIII was the most frequently observed coagulation abnormality, and elevated factor VIII was present in all symptomatic patients. This raises the possibility that factor VIII may serve as a marker of persistent hypercoagulability. Elevated fibrinogen in asymptomatic individuals raises the possibility that fibrinogen could serve as an early marker of thrombotic risk. Obesity and smoking were present in some participants, suggesting that modifiable risk factors may interact with genetic susceptibility.

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