

DEDICATION

To my mother.....

To the soul of my father.....

To my Siblings.....

To my beloved wife and daughter.....

ACKNOWLEDGMENT

First and Foremost praise is to ALLAH, the Almighty, the greatest of all, on whom ultimately we depend for sustenance and guidance. I would like to thank Almighty Allah for giving me opportunity, determination and strength to do my research.

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Abstract

Background: Deep venous thrombosis (DVT) is one of two manifestations of venous thromboembolism (VTE). VTE is a life threatening disease resulting from multiple interactions between different genetic and environmental factors.

Aim: This study aimed to detect the prevalence of factor V Leiden 1691G>A and prothrombin 20210G>A polymorphisms in deep vein thrombosis patients, the coagulation profile and to investigate the role of non-genetic risk factors in the manifestation of DVT.

Methods: A total of 192 Sudanese subjects were examined, including 100 DVT patients and 92 healthy controls. Demographic and clinical data were collected using a structured questionnaire. Citrated blood samples of patients and controls were used for coagulation assays PT, APTT, D-dimer Activated protein C resistance and prothrombin fragments1+2. DNAs isolated from EDTA-blood samples were used for the detection of Factor V Leiden 1691G>A and prothrombin 20210G>A polymorphisms using standard and multiplex polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) analysis.

Results: This study included a total of 100 patients (25 males, 75 females) with proven DVT diagnosis and 92 healthy controls (31 males, 61 females). No significant differences in the prevalence of DVT were detected between males and females ($p = 0.185$). The mean age of the patients was 41.60 ± 17.28 years, while that of controls was 31.65 ± 10.08 years. Ninety-three percent of the DVTs were localized in the left leg and 7% in the right leg. Additionally, 88% of the DVTs were proximal and

12% were distal. Immobility status and cardiovascular disease were the most significantly associated with age ($p < 0.001$). Among the 75 DVT women enrolled in the study, risk factors that most significantly affected younger female patients were pregnancy and oral contraceptive usage. Significant differences were observed between DVT patients and healthy controls in the levels of prothrombin fragments 1+2 ($p < 0.0001$), PT ($p < 0.0001$), APTT ($p < 0.0001$), and D-dimer ($p = 0.044$). Of all subjects, none of the 192 subjects carried the factor V Leiden 1691G>A or prothrombin 20210G>A mutations.

Conclusion: No significant differences in the prevalence of DVT between male and female patients in comparison with healthy subjects. D-dimer and prothrombin fragment 1+2 are considered to be useful for the diagnosis of DVT. Previous history of DVT, immobility status and cardiovascular disease were the most significantly associated with age. Women who are pregnant or in postpartum period and those using oral contraceptives are at a higher risk of developing DVT. Factor V Leiden 1691G>A and prothrombin 20210G>A mutations were not associated with DVT in the Sudanese population examined in this study.

الخلفية: الجلطة الوريدية العميقة (DVT) هي واحدة من اثنتين من مظاهر الجلطات الدموية الوريدية (VTE). الجلطة الدموية الوريدية هي حالة مرضية مهددة للحياة والتي تنتج عن التفاعلات المتعددة بين العوامل الجينية والبيئية المختلفة.

الاهداف: هدفت هذه الدراسة إلى بحث مدى انتشار عامل التخثر الخامس (1691G>A) والبروثرومبين (20210G>A) في مرضى تخثر الأوردة العميقة (DVT) والتحقق في دور عوامل الخطر غير الجينية في حالات تجلط الأوردة العميقة.

الطرق: تم فحص ما مجموعه 192 شخصا سودانيا ، بما في ذلك 100 مريض DVT 92 . تم جمع البيانات الديموغرافية والسريرية باستخدام استبيان م . تم استخدام عينات الدم المزروعة من المرضى والأشخاص الأصحاء لفحوصات تجلط الدم باستخدام انابيب سترات الصوديوم، زمن البروثرومبين، زمن الثرومبوبلاستين الجزئي،-D dimer و شطايا البروثرومبين 1 + 2. تم استخدام الحمض النووي المعزول من عينات دم باستخدام انابيب ثنائي أمين الإيثيلين رباعي حمض الأسيتيك للكشف عن عامل التخثر الخامس (1691G>A) والبروثرومبين (20210G>A) باستخدام تحليل تعدد أشكال الشداف مقيدة الطول (PCR-RFLP) الفردي والمتعدد.

النتائج: شملت هذه الدراسة ما مجموعه 100 مريض بالجلطة الوريدية العميقة (25)

75	92	31	61
الكشف عن عدم وجود فروق ذات دلالة إحصائية في انتشار	وريديّة العميقة بين		
(P = 0.185).	10.08 ± 31.65	17.28 ± 41.60	

7 الساق اليسرى تأثرت وريدية العميقة . 88% من حالات تجلط الأوردة العميقة كانت في الساق اليمنى.

12 القلب والأوعية الدموية هي الأكثر ارتباطًا بالعمر لدى مرضى الجلطة الوريدية العميقة (P < 0.001).

وريديّة العميقة

كبير على النساء الأصغر سنا هي الحمل واستخدام وسائل منع الحمل عن طريق الفم. إحصائية بين المريضات والنساء الأصحاء في مستويات شطايا البروثرومبين 1 + 2 (P < 0.0001) زمن البروثرومبين (P < 0.0001)

الثرومبولاستين الجزئي (P < 0.0001) D-dimer (P = 0.0044) .
الى عدم وجود اي من الطفرات الجينية التي تم التحري عنها تحليل
الشدف مقيدة الطول (PCR-RFLP) لدى جميع المشاركين.
الخلاصة: لا توجد فروق ذات دلالة إحصائية في انتشار الجلطة الوريدية العميقة بين الذكور
D-dimer شظايا
البروثرومبين 1 + 2 مفيدة لتشخيص الإصابة بجلطات الأوردة العميقة.
ان الاصابة السابقة بالجلطة الوريدية العميقة وانعدام الحركة وأمراض القلب والأوعية الدموية
هي
فترة ما بعد الولادة والذين يستخدمون وسائل
منع الحمل عن طريق الفم أكثر عرضة لخطر الإصابة بتجلط الأوردة العميقة.
واخيرا توصلت الدراسة الى ان عامل التخثر الخامس (1691G>A)
والبروثرومبين (20210G>A) لا علاقة لها بالاصابة بالجلطات الوريدية العميقة في المرضى
السودانيين الذين تم دراستهم من خلال هذا البحث.

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List of Abbreviations

A	Arginine
AL	Allelic leader
APC	Activated protein C
APCR	Activated protein C resistance
aPTT	Activated partial thromboplastin time
ARIC	Atherosclerosis Risk in Communities Study
AT	Antithrombin
BMI	Body mass index
CDC	The Centers for Disease Control and Prevention
CHC	Combined hormonal contraceptives
CHS	Cardiovascular Health Study
CI	Confidence interval
CKD	Chronic kidney disease
CVD	Cardiovascular disease
DD	Ddimers
DEPC	Diethyl pyrocarbonate
DNA	Deoxyribonucleic acid
DVT	Deep vein thrombosis
EDTA	Ethylenediamine tetraacetic acid
ELISA	Enzyme-linked immunosorbent assays
EPCR	Endothelial cell protein C receptor
EPCR	Endothelial protein C receptor

ESRD	End-stage renal disease
EU	European Union
G	Glutamin
HDL	High density lipoprotein
HT	Hormone treatment
INR	International normalized ratio
LA	Lupus anticoagulant
LDL	Low density lipoprotein
LETS	Leiden Thrombophilia Study
LMWH	Low molecular weight heparin
NA	Not applicable
NHDS	National Hospital Discharge Survey
OAC	Oral anticoagulant
OC	Oral contraceptive
PAI	Plasminogen activator inhibitor
PCR	Polymerase chain reaction
PE	Pulmonary embolism
PL	Platelets
PPP	Platelets poor plasma
PT	Prothrombin time
RBC	Red blood cell
REGARDS	Reasons for Geographic and Racial Differences in Stroke study
RFLP	Restriction fragment length polymorphism

RVV	Russel viper venom
SD	Standard deviation
SF	Soluble fibrin
TAFI	Thrombin activatable fibrinolysis inhibitor
TF	Tissue factor
TFPI	Tissue factor pathway inhibitor
TM	Thrombomodulin
t-PA	Tissue plasminogen activator
UFH	Unfractionated heparin
US	United states
UTR	Untranslated region
VT	Venous thrombosis
VTE	Venous thromboembolism
vWF	Von Willebrand factor
WHO	World Health Organiztion