

Risk factors for venous thromboembolism at the University College Hospital, Ibadan.

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Abstract

Background: Venous thromboembolism (VTE) possesses a significant public health challenge as it is responsible for high morbidity and mortality rates worldwide. Risk factors play a major role in its pathogenesis. VTE risk factors identification and thromboprophylaxis will reduce the burden of disease and its treatment cost. The study aimed to review the pattern of presentation, and identify risk factors in VTE patients at the University College Hospital (UCH), Ibadan.

Methods: This is a retrospective study of the hospital records of 98 confirmed VTE patients managed at UCH, Ibadan over 18 months. Demographic data and risk factors documented in the case-note were retrieved. Microsoft excel version 2013 and SPSS version 23 were employed for the statistical analysis.

Results: Ninety-eight patients were studied with M: F of 1:1.6. The age range was between 15 and 87 years with a mean age of 52±17years. Seventy-one patients (72%) had DVT. Immobilization was the most frequently identified risk factor, followed by a prior diagnosis of malignancy (15.4%).

Conclusion: This study further confirms immobilization as the most identifiable risk. Others include malignancies and iatrogenic causes by femoral cannulation.

Keywords: Venous thromboembolism, deep vein thrombosis, pulmonary embolism, immobilization

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Facteurs de risque de thromboembolie veineuse dans l'hôpital du Collège Universitaire d'Ibadan

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Résumé

Contexte général de l'étude: La thromboembolie veineuse (TEV) représente un défi de santé publique important car elle est responsable de taux élevés de morbidité et de mortalité dans le monde. Les facteurs de risque jouent un rôle majeur dans sa pathogenèse. L'identification des facteurs de risque de TEV et la thromboprophylaxie réduiront le fardeau de la maladie et son coût de traitement. L'étude visait à examiner le schéma de présentation et à identifier les facteurs de risque chez les patients atteints de TEV dans l'hôpital du collège universitaire (HCU), Ibadan.

Méthode de l'étude: Il s'agit d'une étude rétrospective des dossiers hospitaliers de 98 patients confirmés de TEV pris en charge à l'HCU d'Ibadan pendant 18 mois. Les données démographiques et les facteurs de risque documentés dans la note de cas ont été récupérés. Microsoft Excel version 2013 et SPSS version 23 ont été utilisés pour l'analyse statistique.

Résultat de l'étude: Quatre-vingt-dix-huit (98) patients ont été étudiés avec un M : F de 1 : 1,6. La tranche d'âge était comprise entre 15 et 87 ans avec un âge moyen de 52 ± 17 ans. 71 patients (72 %) avaient une DVT. L'immobilisation était le facteur de risque le plus fréquemment identifié, suivi d'un diagnostic antérieur de malignité (15,4 %).

Conclusion: Cette étude confirme en outre que l'immobilisation est le risque le plus identifiable. D'autres incluent les tumeurs malignes et les causes iatrogènes par canulation fémorale.

Mots-clés: Thromboembolie veineuse, thrombose veineuse profonde, embolie pulmonaire, immobilisation

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INTRODUCTION

Venous thromboembolism (VTE) is a vascular disease characterized by formation of blood clot most often in the deep veins of the leg, groin or arm and travels in the circulation, lodging in the lungs though it can occur as a distinct entity in the lungs (1). It is known as deep vein thrombosis, DVT when it involves the deep veins of the upper and lower limbs and as pulmonary embolism, PE when the lung is involved. It is the 3rd most common vascular disease, though commoner in the elderly (2). It has an incidence of about 0.1% annually in the middle aged but the incidence increases to nearly 1% in the elderly in their ninth decade of life (3,4). Venous thromboembolism remains undiagnosed in about 50% of cases but may present acutely with fatal or life-threatening complications and potential long-term complications such as recurrent venous thromboembolism, post thrombotic syndrome, and chronic thromboembolic pulmonary hypertension (5)

It is reported to be more prevalent in blacks with overall incidence that is about 60% higher in blacks than in whites, the incidence of pulmonary embolism and pregnancy associated venous thromboembolism are found also to be higher in blacks compared to Caucasians (1,3). Pulmonary embolism is reported to be responsible for about 20% of deaths in the hospital and may also contribute to the cause of death in many patients (3,6). The relationship between DVT and PE is such that each can present as a distinct entity or the presence of DVT increases the risk of developing PE (7).

The pathogenesis of thrombosis was first described by Virchow in 1856, he described the contributing factors as a triad. The components of this triad include venous stasis, vascular injury, and hypercoagulability. Stasis is the most important of the components, but stasis alone cannot sufficiently cause thrombosis (8). However, the concurrent presence of venous stasis and vascular injury or hypercoagulability greatly increases the risk for clot formation (9). Venous thrombosis tends to occur in some specific areas such as the pockets close to valves in the deep veins, this is because there is reduced blood flow. Hypercoagulable microenvironment also occurs around the valves and subsequently downregulate certain antithrombotic proteins like thrombomodulin and endothelial protein C receptor.

Venous thromboembolism is a disease with major public health challenges as it is

responsible for high morbidity and mortality worldwide. The long-term complications can reduce quality of life and increase health care expenditures. The management of thromboembolism includes the use of traditional anticoagulants with close monitoring of coagulation profile and the new oral anticoagulants for at least 3-6 months or longer depending on the risk of recurrence. An earlier study on our patients showed that 18% developed DVT despite being on prophylactic anticoagulants, unfortunately studies on inherited causes were not available (10). Current opinion holds that background genetic abnormalities exist in almost all patients with thrombo-embolic disorder. It is known that among normal healthy population, 8.5% have low antithrombin activity (11). Risk factors play a major role in the pathogenesis of venous thromboembolism. (12) These risk factors are either modifiable (acquired) or non-modifiable (genetic). The acquired and genetic factors interact to increase the risk. These risk factors culminate into the three contributing factors of Virchow's triad. For patients on prolonged admission or long distance travelling, the contributing factor will be stasis in addition to any other component of the triad. It is expensive to manage venous thromboembolism in Nigeria but identifying the risk factors and offering thromboprophylaxis and lifestyle modification to patients with risk factors will reduce the disease and financial burden. This study reviewed the occurrence of known risk factors for venous thromboembolism in our environment with the aim that the data generated will form the basis for developing appropriate thromboprophylaxis protocols.

MATERIALS AND METHODS

This is a retrospective, cross sectional, descriptive study of the hospital records of confirmed VTE patients (using Doppler ultrasound scan for DVT and CT-Pulmonary Angiography for PE). These patients were diagnosed and managed at the university college hospital, Ibadan between July 2016 and December 2017. The case notes of only ninety-eight patients were retrievable and were all included in the study. Parameters extracted from the case notes of these patients included the age, gender, type of VTE, site of thrombosis, primary diagnosis, length of stay in the hospital and interventions in the hospital.

The University College Hospital is the foremost tertiary hospital with capacity to admit

1000 patients. The hospital offers services in Surgery, Medicine, Paediatrics, Obstetrics and Gynaecology, Radiodiagnosis, Dentistry, Psychiatry, General Practice, Community Medicine and their subspecialties. The pathology services include Morbid Anatomy/Histopathology, Medical Microbiology, Chemical Pathology and Haematology. The haematology department in collaboration with pulmonology unit of internal medicine attends to patients with pulmonary embolism except in severe cases where intensive care unit care is needed in which case the anaesthetists are involved. Deep vein thrombosis is however solely managed by the department of Haematology. These patients were treated for three to six months based on the type of VTE.

Microsoft excel version 2013 and SPSS version 23 were employed for the statistical analysis. Frequency, mean, and standard deviation were determined for variables. Descriptive statistics were used to analyze characteristics of participants. Continuous variables, were analyzed by mean and standard deviation (SD). Categorical variables, were considered in terms of frequency and percentage.

As the study was retrospective and completely de-identified, such that the information was not attributable to any of the patients, ethical approval was not sought.

RESULTS

The study group included 38 males and 60 females (M: F=1:1.6). Their age ranged between 15 years and 87 years with a mean age of 52 ± 17 years. Only nine patients (9.2%) were less than 30 years while 39 patients (39.8%) were within 30-50 years, others were above 50 years (Figure 1).

Seventy-one patients (72.4%) had deep vein thrombosis only while 17 patients (17.3%) had PE only, seven patients (7.1%) had both DVT and PE. The remaining two patients (2.04%) had thrombosis in other sites.

Out of seventy- nine patients with deep vein thrombosis, only one of them, (1.3%) had distal deep vein thrombosis, 46 patients (58.2%) had proximal deep vein thrombosis in the left lower limb while 21 (26.6%) had right proximal deep vein thrombosis and 11 patients (13.9%) had bilateral proximal deep vein thrombosis. There was no patient with bilateral distal deep vein thrombosis. This is shown in Fig 3.

Immobilization, in 47 patients (48%) was the most commonly identified risk factor, followed by malignancies in 13 patients (15.4%)

and femoral cannulation for haemodialysis in 11 patients (12.3%). Malignancy was the commonest identifiable risk in those with bilateral DVT, which was observed in 10 patients with bilateral deep vein thrombosis. The common causes of immobilization were neurosurgical admission for traumatic myelopathy, orthopaedic admission for femoral fractures and surgeries (caesarean section and myomectomy) (Figure 2).

DISCUSSION

Risk factors, either modifiable or non-modifiable, play a major role in the pathogenesis of venous thromboembolism. In this index study, ninety-eight patients were reviewed, there were more female than male, this could be as a result of pregnancy and other gynaecologic conditions that might increase the risk in women and this is consistent with the study of Kotila et al (2013). However, our finding is contrary to the review done among Caucasians by White RH (2003) which reported no sex predilection for venous thromboembolism (12).

The age range of the index study group is 17-85 years and mean age is 52 ± 17 years, the very low age limit of 17 years is as a reflection of few of the patients with inherited risk factors, protein S deficiency. This is because patients with natural anticoagulant deficiencies like protein S deficiency present in early adulthood (5). The age distribution of the study group showed that more than half of the patients are above 50 years old, this corresponds with the age range at which most chronic diseases develop. This finding agrees with previous studies done in our centre which showed the median age of 53 years and equally consistent with other previous studies that showed that there is increasing incidence of VTE with increasing age (3,4,13).

The incidence of pulmonary embolism in this study is higher than previously reported, even though as with previous studies DVT is more prevalent. (10,11). The study by White RH 2003 may not be comparable because it was an autopsy finding that showed incidence of PE to be as high as 55% in their studies that included autopsy. This study suggests that distal DVT is uncommon is our setting as about 2% of patients with DVT presented with distal deep vein thrombosis. The fact that isolated distal DVT could be easily missed clinically (14) may contribute to this finding. This finding differs from the previous study done by Helia Robert-Ebadi and Mara Righini (2017) where calf DVT was said to constitute 30-50% of DVT (15).

Also, about 60% of the patients had left

proximal deep vein thrombosis, this is consistent with previous studies that showed increased left proximal deep vein thrombosis. The left limb was affected in 61% of patients Vs 29% affecting the right limb (10, 16,17). Iliac vein compression has been found to be associated with increased risk of left-sided DVT, this is because there will be stasis of blood in the iliac vein.

Immobilization is an established risk factor for VTE, however being associated with VTE in about half of the patients increases the need to work out more aggressive preventive measures that would reduce the occurrence of VTE. Gender and age distribution are not modifiable but immobilization could be influenced to reduce the vulnerability of patient in developing DVT. Similar to report by Abah JP et al, this immobilization was as a result of prolonged bed rest during admission in patients with CNS injury and post- surgery, long distance travel (18). Immobilization causes stasis of the blood, one of the components of virchow's triad and triggers thrombus formation in the deep veins.

About 15% of the patients had Cancer Associated Thrombosis, this is because cancerous cells can initiate thrombosis and can also compress the veins. This finding is in agreement with 12% reported by kotila et al but contrary to previous study by Blom JW et al which showed that only 1.2% of patients with malignancies develop Cancer Associated Thrombosis. The difference might be due to variation in study population, study site and stage of the malignancy (19). Advances in medical treatment could alter the epidemiology of DVT as suggested by 12% of the patients studied who had DVT associated with femoral cannulation for haemodialysis in patients with end stage renal disease. The cannulation causes vascular injury, a component of the virchow's triad that leads to thrombus formation. The hypercoagulable state in renal disorder, is also a contributing factor responsible for thrombus formation in these category of patients (20). Limitation of this study is the study being a retrospective study with missing of case records of some VTE patients, this affected the sample size.

CONCLUSION

This study further reinforces association between immobilization and development of DVT. Other risk factors include malignancies and iatrogenic cause, femoral canulation. These risk factors are modifiable and efforts should be directed at identifying all these risk factors in

patients at presentation and possibly commence patients on prophylactic anticoagulation, physiotherapy and allow for early ambulation to prevent VTE.

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Conflict of interest: The authors declare no competing interests

Authors' contributions: OWA, OAA, IDN, SPO, and FAF were involved in conceptualization, data gathering and analysis, and interpretation of result. OWA, CCA, FAF and JAO were involved in writing and review of the manuscript. All authors have read and given final approval of the version to be published.

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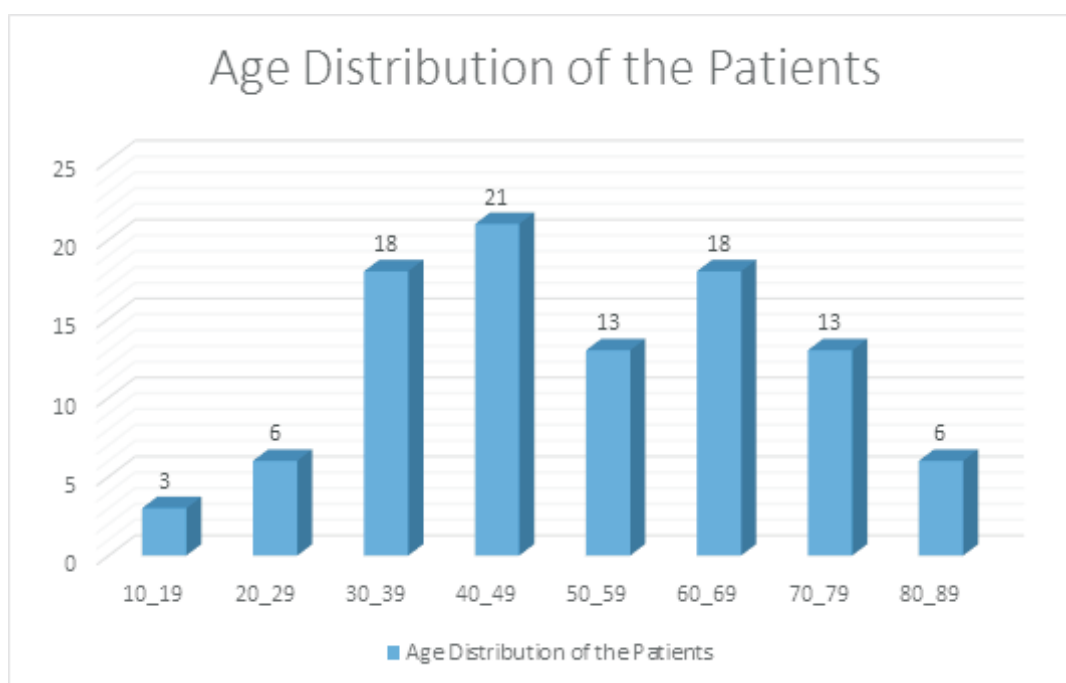


Figure 1: Age Distribution of Patients with Venous Thromboembolism

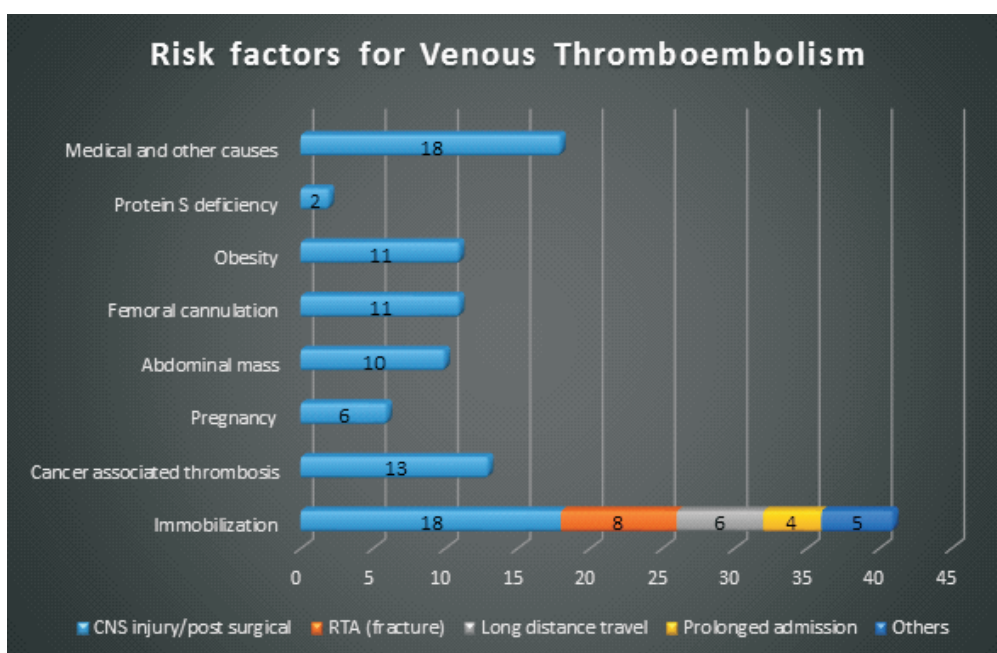


Figure 2: Risk factors for Venous Thromboembolism

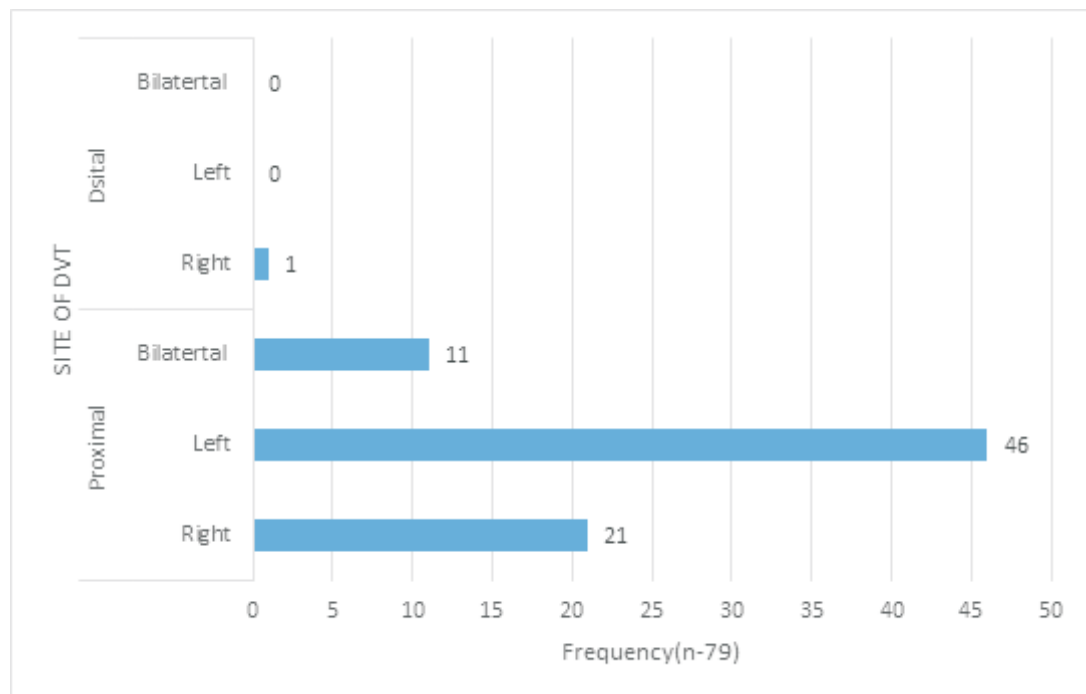


Figure 3: Site of Thrombosis in Patients with Deep Vein Thrombosis