CLINICAL RISK FACTORS FOR DEEP VEIN THROMBOSIS IN MAIDUGURI, NIGERIA

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SUMMARY

Objective: To study the pattern of deep vein thrombosis (DVT) and associated clinical risk factors in Maiduguri, Nigeria, with the aim of recognizing common risk factors and the need for prophylactic intervention.

Materials and Methods: Twenty-two (22) cases of DVT seen at the University of Maiduguri Teaching Hospital (UMTH) from 1996 to 1999 were retrospectively analysed with respect to the pattern of DVT and associated clinical risk factors as documented at diagnosis.

Results: The frequencies of individual risk factors among the 22 patients studied included obesity in 15 (68%) patients, abdominal operation in 6 (27%) patients, pelvic operation in 5 (23%) patients, advancing age greater than 45 years in 4 (18%) patients, puerperium in 4 (18%) patients, SCD in 2 (9%) patients, HIV infection in 2 (9%) patients and SLE in 1 (5%) patient. No risk factors were identified in 2 (9%) patients. The left lower limb was affected in 77% of cases while the remaining 23% of cases had right lower limb DVT. Proximal (iliofemoral) DVT was seen in 64% of cases while the remaining 36% of cases had distal (calf) DVT.

Conclusion: Proximal venous thrombosis affecting the left lower limb is the predominant clinical pattern of DVT in this study, while obesity, surgery, puerperium and advancing age are the commonest associated risk factors in the affected patients. There is therefore the need to consider prophylactic anticoagulation for puerperal and post-operative patients especially in those who are obese or older than 45 years.

KEY WORDS:
DEEP VEIN THROMBOSIS, RISK FACTORS

INTRODUCTION

The normal vascular endothelium is non-reactive with circulating platelet and coagulation factors[1-3]. It is postulated however, that low levels of activated factors X and V are continuously generated, apparently spontaneously, within normal blood vessels[4]. These factors lead to generation of a small amount of thrombin, but this is normally rapidly inactivated by the serine protease inhibitor antithrombin III[4]. The effect of Antithrombin III is potentiated by the action of other naturally occurring inhibitors of coagulation such as protein C and protein S, which in the presence of thrombomodulin oppose thrombin generation by inactivating FVa and FVIIIa[5-8]. In addition, Protein C has profibrinolytic properties, which facilitates the digestion of any fibrin nidus that might have been generated by thrombin, thereby preventing the establishment of intravascular thrombi[3, 9,10]. These normal haemostatic mechanisms maintain a critical thrombo-haemorrhagic balance, which ensures that blood remains in fluid state within vessels without undue bleeding or thrombus formation[1]. However, patients who have defects or abnormalities that alter the thrombo-haemorrhagic balance in favour of fibrin deposition are at increased risk of venous thrombosis[1]. Such patients are considered to have thrombophilia[1], a term used to describe acquired or familial disorders of the haemostatic mechanisms that are likely to predispose to thrombosis.

Venous thrombosis becomes more common as the age advances beyond 45 years, and its occurrence is frequently associated with acquired risk factors, such as trauma, surgery, obesity, varicose veins, pregnancy, hyperviscosity, or systemic lupus erythematosus (SLE)[1]. Thrombosis, however, may develop at a younger age in the absence of easily identifiable acquired risk factors. Such patients are likely to suffer from familial thrombophilia and may have congenital deficiencies of the natural anticoagulants such as antithrombin III, Protein C or Protein S[1].

The clinical manifestations of DVT include unilateral or bilateral swelling of the lower limbs, which may be associated with pain, warmth and tenderness over the course of posterior tibial vessels [2,3]. However, caution must be exercised in making clinical impressions as unilateral cases must be carefully differentiated from cellulitis, thigh and calf muscle tears, while bilateral cases must be distinguished from pedal oedemas due to congestive cardiac or renal failure[2, 3, 11,12]. Homan's sign may be positive in some cases of DVT[2, 3]. However, this procedure is associated with the risk of dislodging venous thrombi that can lead to embolic complications and hence eliciting the Homan's sign is no more desirable as a clinical procedure in assessing patients with DVT[2, 3]. Patients with DVT may show prominent collateral superficial veins in the affected limbs[2, 3,11,12]. Peripheral arterial pulses are usually present except in late cases when they may be absent and pre-gangrenous changes may set in [2,3, 11, 12]. Pyrexia may be present in some cases and is sometimes an important feature of occult cases of DVT[2, 3, 11,12].

In this report we present the pattern of deep vein thrombosis (DVT) and its associated risk factors as seen at the University of Maiduguri Teaching Hospital (UMTH), Maiduguri, North East Nigeria. The study is aimed at recognizing common risk factors and the need for prophylactic intervention.

PATIENTS AND METHODS

A retrospective analysis of 22 patients with DVT managed by the Department of Haematology of UMTH was carried out. All cases were inpatients and were either primarily Haematology patients or primarily managed by other clinical departments on whom Haematologist's consultations were secondarily requested. The study period spanned four years from 1996 to 1999. Information regarding patients' age, weight, height, medical and surgical clinical risk factors, affected limb and vascular locations of thrombi were retrieved from patients' case notes in each case. In all cases the diagnosis of DVT was based on clinical features such as swelling, pain, warmth and tenderness over the course of posterior tibial vessels of the affected limbs and was subsequently confirmed by contrast radiographic venography thereby defining the location of the thrombi, which were identified as intra-luminal filling defects[2, 3].

Every effort was made to obtain key clinical data on all patients, however, as limitation of any retrospective study some of such data may not be available and absence of control group is another draw back of retrospective studies. A total of 7 patients seen during the period under review in whom venography was not performed were excluded from this study.

For each patient the body mass index (BMI)[4] was calculated from the formula: weight (kg) divided by the square height (m) i.e kg/m^2 The normal range of BMI was taken to be 20-25 and a patient is considered to be obese if the BMI is greater than 30 kg/m^2 .

RESULTS

Twenty-two (22) patients with DVT were seen in the department of Haematology of UMTH, Maiduguri from 1996 to 1999. The patients' ages ranged from 28 to 54 years (mean age, 41years). Multiple risk factors were seen in 15(68%) patients and single risk factors were observed in 5(23%) patients The frequencies of individual risk factors among the 22 patients studied are as shown on Table 1, which included obesity in 15 (68%) patients, abdominal operation in 6 (27%) patients, pelvic operation in 5 (23%) patients, advancing age greater than 45 years in 4 (18%) patients, puerperium in 4(18%) patients, SCD in 2 (9%) patients, HIV infection in 2 (9%) patients and SLE in 1 (5%) patient. No risk factors were identified in 2 (9%) patients.

The cases of abdominal operations encountered in this study included 4 cholecystectomies, 2 appendectomies and 1 laparatomy for bullet injury; while the pelvic operations included 3 caesarian sections and 2 hysterectomies. None of our cases had any malignant diseases.

Clinical features of DVT in the surgical and puerperal patients developed within the first 10 and 14 post-operative and post-natal days respectively.

The left lower limb was affected in 17(77%) patients while the right lower limb was affected in the remaining 5(23%) patients. Proximal (iliofemoral) DVT was seen in 14(64%) patients while the remaining 8(36%) patients had distal (calf) DVT.

TABLE 1: FREQUENCIES OF RISK FACTORS IN 22 PATIENTS WITH DVT

RISK FACTORS	No OF PATIENTS AFFECTED (%)
Obesity.	15 (68)
Abdominal operation.	6 (27)
Pelvic operation.	5 (23)
Advancing age > 45.	4 (18)
Puerperium.	4 (18)
Sickle Cell Disease.	2 (9)
HIV Infection.	2 (9)
Systemic Lupus Erythematosus.	1 (5)
Unidentified.	2 (9)

DISCUSSION

Obesity was identified as a risk factor in the majority (68%) of patients with DVT. Obesity is an important risk factor for the development of DVT because it restricts physical activity and respiratory excursions, which lead to reduction in venous return resulting in venous stasis and formation of thrombi[2, 11]. The high prevalence of obesity in our patients underscores the clinical significance of obesity as a major risk factor in our subjects.

The second must important identified risk factor for DVT were surgical procedures, including abdominal and pelvic operations, which were associated with 50% of the patients studied. Many factors contribute to the development of DVT in the post-operative period. They include venous stasis due to immobilization, reduction in muscle pump activity in the lower limbs and diminished respiratory activity leading to reduction in negative intra-thoracic pressure[11-13]. Furthermore, surgical patients are particularly prone to DVT due to increased tendency to hypercoagulability of blood in the postoperative period as a result of raised levels of fibrinogen and other coagulation factors as well thrombocytosis[12, 13]. There is therefore the need to counteract these factors by early post-operative ambulation in order to prevent the development of DVT in the post-operative period[11].

Advancing age beyond 45 years was identified as a clinical risk factor in only 18% of our patients. However, these patients need special consideration because they are particularly prone to DVT, which may be recurrent especially if they are immobilized by age-related illnesses such joint and heart diseases[1, 11]. Further more, other risk factors for DVT may assume greater significance as the age advances and this is particularly so in individuals are aged 60 years[1, 11]

Puerperium was identified as a risk factor in 18% of our DVT cases. The puerperium is a period when patients are prone to DVT due to pregnancy-induced hypercoagulability attributable to enhanced platelet responsiveness, raised levels of coagulation factors, (particularly factors VII, VIII, vWF and fibrinogen) and impaired fibrinolysis[2, 3].

Only one (5%) of our patients had SLE and a pre-anticoagulation clotting screen at the time of diagnosis of DVT suggested the presence of lupus anticoagulant (LA). This is typically characterized by a normal prothrombin time (PT) and a prolonged activated partial thromboplastin time (APTT), which could not be corrected by addition of normal plasma[14]. The LA is an antiphospholipid antibody, which prolongs phospholipid-dependent tests such as PTTK[14]. Paradoxically, however, it causes recurrent venous and arterial thrombo-embolism and recurrent abortions[15, 16]. The mechanism of thrombosis due to LA is not completely understood but may be associated inhibition of protein C activation by thrombomodulin[17, 18].

Sickle cell disease (SCD) was identified as a risk factor for DVT in 9% of our patients who were known cases of sickle cell anaemia. In one of these patients, DVT occurred during bone pain crisis while in the other it occurred in steady state. Although DVT is not commonly seen in SCD patients, SCD is a recognized risk factor for venous thrombosis because sickling increases blood viscosity[19]. Furthermore, sickling causes endothelial damage, leading to exposure of sub-endothelial structures and platelet activation and adhesion, which add to the risk of thrombosis especially in the presence of thrombocytosis commonly seen in SCD[20, 21]. The tendency for venous thrombosis may be higher during vaso-occlusive crises in view of the poor state of hydration and reduction in mobility. Moreover recent studies revealed that sickled erythrocytes increase endothelial cell production of adhesion molecules, which create a vascular environment that favours cellular adhesion and prolongation of microvascular transit time, thereby increasing the chances of thrombi formation[22].

Two (9%) patients were previously diagnosed cases of HIV infection with AIDS-related complex. There were no obvious risk factors for DVT in these patients. However, the pre-anticoagulation clotting profiles of these patients were suggestive of the presence of lupus anticoagulant (LA) manifesting with normal PT and prolonged APTT not correctable by a mix with normal plasma[14]. In fact, LA had been reported in 80% and 10% of North Americans with symptomatic and asymptomatic HIV infection respectively[23, 24]. It would therefore appear that the LA might be a predisposing factor for DVT in the two HIV patients in our series. A detailed and wider study of the haemostatic changes in Nigerian patients with HIV infection will help to identify those factors that are important in the causation of DVT in this subset of patients.

In two (9%) of our patients (Table 1) no obvious clinical risk factors for DVT could be identified and both patients had normal pre-anticoagulation clotting profiles including PT and APTT. Both patients were males under the age of 30years. Although there was negative family history of DVT from both patients, detailed investigations for genetic thrombophilic disorders such as Antithrombin III, Protein C and Protein S assays, which unfortunately were not performed due to limitations of laboratory facilities, might have been useful in detecting the probable factors in these cases.

The left lower limb was affected in 77% of our patients, while only 23% of cases presented with right lower limb involvement. The higher incidence of DVT in the left lower limb could be attributed to the compression of the left common iliac vein at the origin of the left common iliac artery thereby increasing venous stasis, thus favouring the development of DVT in the left lower limb[11].

The most commonly affected vessels in our patients were the iliofemoral veins accounting for 64% of cases while 36% occurred in the calf (soleal) veins. The clinical significance of this finding is the fact that DVT in proximal veins such as the iliofemoral, carries higher risk of pulmonary embolism and post thrombotic syndrome than that confined to the calf veins[25, 26]. Our finding is at variance with previous reports, which suggested that DVT of the legs occurs more frequently in the calf than the proximal veins[11]. Therefore, the majority of our patients were at high risk of thrombo-embolism, a phenomenon that was thought to be uncommon in Africans[11, 25, 26]. However, with increasing level of awareness and availability of diagnostic facilities, thrombo-embolism is becoming increasingly recognized as a significant cause of morbidity and mortality among Nigerian patients[27]. In fact, a recent study in Jos showed that venous thrombo-embolism was responsible for about 2% of hospital deaths in the surgical wards[27]. There is therefore a need for applying preventive measures including prophylactic anticoagulation and early post-operative ambulation aimed at preventing the development of

DVT in susceptible patients; such measures will also surely bring down the rate of venous thrombo-embolism with its attendant serious morbidity and mortality.

CONCLUSION

Proximal venous thrombosis affecting the left lower limb is the predominant clinical pattern of DVT in this study, while obesity, surgery, puerperium and advancing age were the commonest associated risk factors in the affected patients. There is therefore the need to consider prophylactic anticoagulation for puerperal and post operative patients especially in those who are obese or older than 45 years. More over, early post-operative ambulation should be encouraged in all surgical cases in order to minimize the risk of DVT. Further more, patients with other risk factors such as SLE and sickle cell disease may also need prophylactic anticoagulation if subjected to additional thrombotic risks factors such as surgical operation. The relationship between HIV infection, lupus anticoagulant and DVT needs further evaluation.

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