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A revisit of venous thromboembolism

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Abstract

Objective: To determine the effect of the introduction of Doppler ultrasonography to the management of venous thromboembolism in a health care facility in Nigeria.

Method: A descriptive study of cases of venous thromboembolism (VTE) over a five year period (March 2007-February 2012) was compared with a five year review done two decades ago before the introduction of Doppler ultrasonography.

Results: This review showed an increase of VTE cases from 60 to 178 with a median age of 53yrs, median age of female patients was 5yrs younger than male patients with Male/female ratio of 1:1.2. There was an even distribution of patients seen over the five year period with a mean prevalence of 35.6 patients per year. Patients with distal deep vein thrombosis (DVT) were in the majority (76%) compared with proximal DVT and PE which were 21% Vs 3%. About 4% of the patients had a recurrence of the VTE with male patients having twice the likelihood of a re-thrombosis. Common co-morbid states observed are cerebrovascular disease (14.5%), cancers (12.2%), retroviral disease (6.7%) and diabetes (6.2%). Prostatic cancer was more common than other cancers while patients with retroviral disease are more likely to have an extensive DVT.

Conclusion: The introduction of Doppler ultrasonography increased the awareness and diagnosis of VTE, we suggest that patients with associated disease conditions are placed on prophylactic anticoagulation, it is also necessary to determine the prevalence of inherited causes of VTE in the population.

Keywords: *Embolism, iliofemoral, prophylaxis, therapeutic, anticoagulation*

Résumé

Objectif: Déterminer l'effet de l'introduction de l'échographie-Doppler pour la gestion de la maladie thromboembolique veineuse dans les centres de santé au Nigeria.

Méthode: Une étude descriptive des cas de thromboembolie veineuse (TEV) sur une période de cinq ans (Mars 2007-Février 2012) a été comparée à un examen quinquennal fait, il ya deux décennies avant l'introduction de l'échographie-doppler.

Résultats: Cette étude a montré une augmentation des cas d'ETEV de 60 à 178 avec un âge moyen de 53 ans. L'âge moyen des patientes était de 5 ans plus jeune que chez les hommes ayant un rapport mâle / femelle de 1:1,2.La répartition des patients examinés au cours de la période de cinq ans était homogène avec une fréquence moyenne de 35,6 patients par an. Les patients atteints de thrombose veineuse distale profonde (TVP) étaient en majorité 76% par rapport à une TVP proximale et le PE était de 21% contre 3%. Environ 4% des patients ont eu une récidive de la thromboembolie veineuse chez les patients masculins ayant deux fois la probabilité d'une nouvelle thrombose. Les états fréquents de Co-morbides qui ont été observés sont des maladies cérébraux-vasculaires (14,5%), les cancers (12,2%), la maladie rétrovirale (6,7%) et le diabète (6,2%). Le Cancer de la prostate est plus fréquent que les autres cancers alors que les patients atteints de la maladie rétrovirale sont plus susceptibles d'avoir un vaste TVP.

Conclusion: L'introduction de l'échographie Doppler a augmenté la prise de conscience et le diagnostic de MTEV. Au finish, nous suggérons que les patients atteints de maladies associées aux conditions médicales soient placés sur l'anti-coagulation prophylactique. Il est également nécessaire de déterminer la fréquence des causes héréditaires de la TEV parmi nos populations.

Introduction

A review of the diagnosis and treatment of venous thromboembolism (VTE) which entailed a five year retrospective review of all cases referred to the Haematology Department of the University College Hospital (UCH), Ibadan Nigeria was carried out two decades ago [1]. Attention was drawn to VTE around the time of the study because deficiencies of some natural inhibitors of coagulation were found to result in familial thrombophilia [2,3]. Shortly afterwards mutation in the gene for factor V was found to be associated with resistance to activated protein C [4], factor V Leiden mutation as it is known, is also a cause of familial thrombophilia. All these familial thrombophilia are known to result in thromboembolic disorders especially in young people

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and in its occurrence at unusual sites. We therefore thought it fit to do another review of this subject especially since the institution now has facility for Doppler Ultrasonograpphy, a state of the art equipment for the diagnosis of deep venous thrombosis (DVT). The management of the disorder has also been revolutionized by the use of low molecular weight heparin in its treatment which does not require rigorous monitoring like unfractionated heparin and is less associated with bleeding as a complication [5].

Materials and methods

Patient Recruitment

Data was obtained from the departmental records of all patients referred to the Haematology Department, UCH, Ibadan, Nigeria for both therapeutic and prophylactic anticoagulation over a five year period (March 2007-February 2012). Case definition was the presence of symptoms and signs of VTE and availability of Doppler Ultrasonographic report for DVT while pulmonary embolism (PE) was based on a combination of Chest X ray findings of segmental opacities and at least a sinus tachycardia on Electrocardiography or a pulmonary angiographic report. Patients who were referred to the department for prophylactic anticoagulation because of the use of a pacemaker or other heart conditions were not included in the study. A baseline coagulation profile (Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT)) was a requirement in all patients but this is not often possible for logistic reasons but most patients had a PT/ APTT done twice weekly initially and then weekly while on admission but only PT was done every fortnight for follow up in the outpatient clinic.

Treatment

All patients were initially commenced on low molecular weight heparin (LMWH) or unfractionated heparin if they are unable to afford LMWH. Conversion from heparin to oral anticoagulation therapy (Warfarin sodium) was usually after a three day overlap between the use of both heparin and Warfarin and achievement of the desired international normalized ratio (INR). An INR of 2-3 and 2.5-3.5 were considered satisfactory for DVT and PE respectively. Patients with distal DVT were followed up for a minimum of three months in the outpatient clinic while those with proximal (iliofemoral), extensive DVT or PE were followed up for a minimum of six months. A repeat Doppler Ultrasonography was done in DVT patients before the anticoagulation was discontinued for patients who could afford the test.

Data management

Data were analyzed using SPSS version 16. The age of patients were grouped in decades but all patients who were 30yrs and below were grouped together. Patients who were reported as having extensive DVT by Ultrasonographic report were analyzed along with patients with proximal DVT.

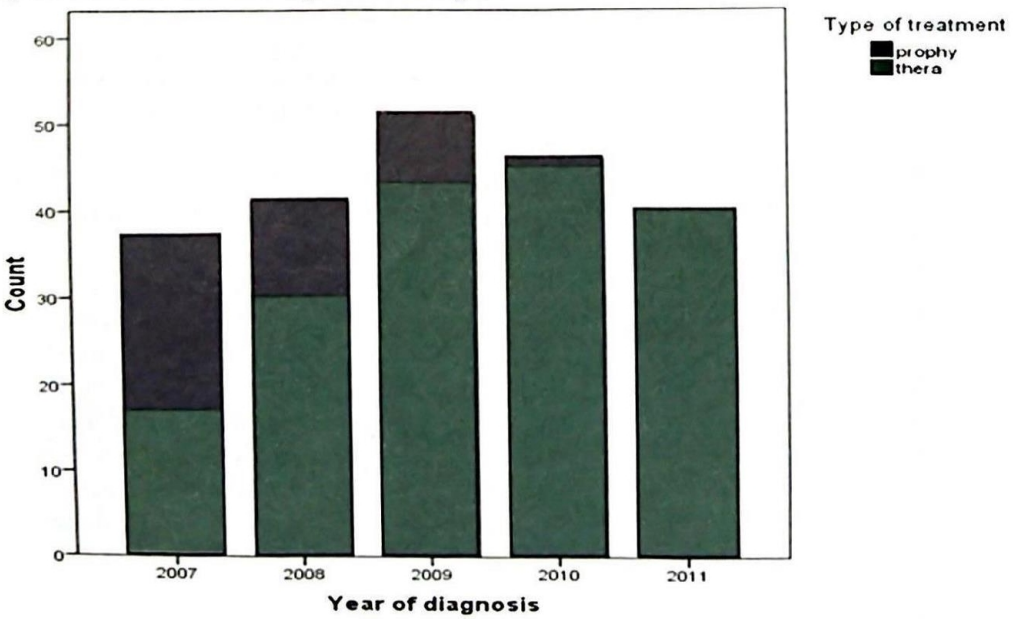

Fig. 1: A comparison of prophylactic and therapeutic anticoagulation over a five year period.
Prophy: Prophylactic anticoagulation
Thera: Therapeutic anticoagulation

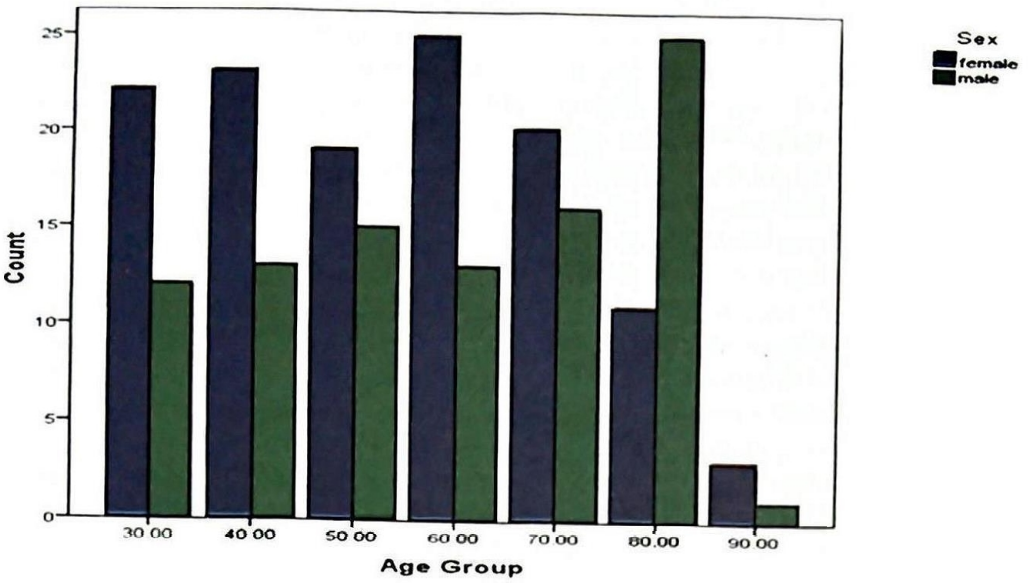

Fig. 2: Sex distribution of VTE over a five year period

Results

Demographics

A total of 221 patients received anticoagulation over the five year period of which 178 were therapeutic and 48 were prophylactic (fig 1), the number of patients with VTE increased gradually from 17 in 2007 to 46 in 2010 and then dipped to 40 in 2011 with an average of 35.6 patients per year. The median age of patients was 53yrs (25th percentile 38yrs, 75th percentile 67yrs), the median age for female patients was 5yrs younger than male patients 49yrs Vs 54yrs. The age range of patients seen was 12-87yrs with a median age group of 41-50yrs, 38 patients were seen in that age group. All other age groups had 36 patients each but 27 and 4 patients were ≤ 30yrs and ≥80 yrs respectively. There was a preponderance of female patients in all the age groups except in the 8th decade where male patients were twice as affected as female patients (fig.2) The overall M:F ratio was 1:1.2.

Clinical data

Patients with distal DVT were in the majority (76%) while those with proximal DVT and PE were 21% and 3% respectively. The left limb was affected in 61% of patients Vs 29% affecting the right limb while 10% had both limbs affected. There was no sex predilection in patients who had both limbs affected. About 4% of the patients had been previously managed for VTE and male patients have twice the likelihood of re-thrombosis than female patients.

Disease association

Patients with Cerebrovascular Disease (CVD) and cancer are more likely to have VTE (Table) with patients with cancer of the prostate in the majority. A high representation of patients with retroviral disease and diabetes (6.7% Vs 6.2%) in this study is worthy of note. Patients with kidney disease constituted 3.3% of the patients out of which 1.4% had nephrotic syndrome.

Clinical states associated with venous thromboembolism

Clinical State	No of Cases	Per-centage
Cerebrovascular Disease (CVD)	25	14.0
Cancers	23	12.9
Retroviral Disease (RVD)	12	6.7
Diabetes	11	6.2
Kidney diseases	7	4.6
Trauma	3	1.7
Pregnancy	3	1.7
Other comorbidities	94	52.2

Management

Patients managed for prophylactic anticoagulation constituted 18% of the study group; these were mostly neurosurgical and orthopaedic patients who are usually hospitalized for a long time before or after surgery. Equal numbers of patients were managed for prophylactic and therapeutic anticoagulation in the 1st year of the study, thereafter there was a gradual decline in the number of patients managed for prophylactic anticoagulation until the last year when all the patients seen were on therapeutic anticoagulation (fig 1).

Discussion

The prevalence of VTE appears to have increased since the last review taking into consideration the fact that venography was the method of diagnosis in the previous review while this present review used Doppler ultrasonography. The rise in prevalence is likely linked to the availability of Doppler ultrasonography which is not an invasive procedure and less associated with mortality like venography, the rising incidence of HIV/AIDS may also be contributory. There were other dissimilarities between the results of both reviews, the observed peak age occurrence in the previous review was absent in the present review which showed similar prevalence in all the age groups except those in the 9th decade, also the median age group for the first review was a decade younger than for the present study. Again, there was no sharp contrast in the male/female ratio in all the age groups in the previous review, and iliofemoral vessels were also more commonly affected than the distal vessels in the said study. Both studies however recorded a higher affectation of the left limb which has been confirmed by other studies [6,7], It is not immediately apparent why the left limb is more affected.

This study also showed that recurrence of VTE was more common among male patients, which has also been reported by other studies [8,9], a review found out that 1% and 0.5% of patients with total/ partial knee arthroplasty and total/partial hip arthroplasty using recommended prophylaxis for VTE were noticed to develop another episode of VTE before discharge [9]. The prolonged hospital stay and duration of surgery in orthopaedic and neurosurgical patients is a reason why the use of prophylactic anticoagulation is more prominent in these specialties. The number of patients for prophylactic anticoagulation gradually declined over the five year period, this is not an indication of less use of prophylactic anticoagulation but may be because these specialties are now used to the management of patients on prophylactic anticoagulation so rarely are such patients referred to Haematologists for specialized care. This is especially so because the dose of Warfarin used at 2.5mg daily would most times give an INR of 1-1.3 which is within normal range.

Evidence has shown that infection with the Human Immunodeficiency Virus (HIV) is associated with the risk of developing venous thromboembolism [10] and a 2-10 fold increase has been noted in comparison with the general population. Age younger than 50yrs, Proteins S and C deficiency disorders, use of protease inhibitor and the presence of opportunistic infections and antiphospholipid antibody are identified risk factors [11]. Most of the identified risk factors were not sought for in our group of patients but only two of the twelve patients with retroviral disease were older than 50yrs, and half of the patients had extensive disease (either as proximal or bilateral involvement). It has therefore been suggested that HIV patients with the identified risk factors should be placed on prophylactic anticoagulation. Co-morbidities involving VTE and diabetes was noted in 6.7% of our cohort of patients but other studies have reported a higher prevalence of 10% [12)] and 12% [13].

Inherited causes of VTE include deficiencies of natural inhibitors of coagulation like Antithrombin III (ATIII), Proteins C and S and factor V Leiden mutation. Deficiencies of these proteins have been found in the occasional patients in our hospital, especially young patients, who could afford the cost of confirming the diagnosis. The even distribution of the disease over the years would suggest an inherited cause especially when the cause is unknown in more than half of the patients. Nephrotic syndrome is known to be associated with VTE because the protein loss associated with the disease is thought to include the loss of natural inhibitors of coagulation especially ATIII [14]. Only three patients with nephrotic syndrome were seen in this review but four other patients with chronic kidney disease or chronic glomerulonephritis were seen. Since protein loss may occur in other disorders of the kidney, it has been advocated that urinalysis be done in patients with VTE [15]. Even though we do not subscribe to this, we would rather suggest that patients with nephrotic syndrome and other kidney diseases be screened for a hypercoagulable state by doing coagulation tests (PT/APTT) and those with a high index of suspicion should then have a Doppler ultrasonography done or that patients who could afford a Doppler ultrasonography should have it done without any prior screening since this may be cost effective on the long run. This will help to prevent this preventable disease with high mortality.

We agree with the conclusion of the former review that VTE is not an uncommon disorder in Nigeria, so there is a need to identify disease conditions associated with it or other predisposing factors so that patients with such disorders could be placed appropriately on prophylactic anticoagulation. It is also necessary to determine the prevalence of inherited causes of VTE in the Nigerian population.

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