

Perception and Practice of Thromboprophylaxis in Patients with Hematological Malignancies among Hemato-oncology Practitioners in Nigeria

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Abstract

Background: Cancer-associated thrombosis is a cause of increased morbidity and mortality in patients with hematological malignancies. Thromboprophylaxis may reduce this risk and improve the patients' prognosis and quality of life. **Objectives:** The study evaluates the awareness and practice of thromboprophylaxis by physicians managing patients with hematological malignancies and identifies challenges with such practice. **Subjects and Methods:** This descriptive cross-sectional study was conducted during the 42nd Annual General Meetings of the Nigerian Society of Haematology and Blood Transfusion held in Lagos 2016. A 12-item pretested questionnaire was used to obtain data on the perception and practice of thromboprophylaxis of hemato-oncologic patients from the 55 consenting hematologists in attendance. Data were analyzed with SPSS version 21. **Results:** The awareness and practice rate of cancer thromboprophylaxis are 96.4% and 92.7%, respectively. Multiple myeloma is the most common neoplasm of which hematologists practice thromboprophylaxis. Warfarin is the most prescribed anticoagulant. Doppler ultrasonography and basic coagulation screening tests are most readily available investigations. Funding and laboratory insufficiency are the leading challenges mitigating against effective management of venous thromboembolism (VTE). **Conclusion:** There is a high level of awareness and practice of thromboprophylaxis in cancer patients by Nigerian hematologists; however, scarcity of fund for investigation and drug procurement and limited laboratory capacity to diagnose and monitor patients still constitute a challenge to effective management of VTE.

Keywords: Hematological malignancy, hematologist, thromboprophylaxis

INTRODUCTION

The association between cancer and venous thromboembolism (VTE) is well established. It is estimated that approximately 20%–30% of all first-time thromboembolic events are associated with cancer.^[1-3] Cancer patients have a several-fold increased risk of VTE compared to the general population or patients without cancer with relative risk ranging from 4-fold to 7-fold.^[4,5] Thrombotic events are a major cause of increased morbidity and the second leading cause of morbidity and mortality in patients with cancer including hematological malignancies.^[6,7]

The risk of thrombosis varies with cancer type, stage of disease, treatment modality, and other patient-related risk factors.^[8] Horsted *et al.*^[9] in their study rated hematologic neoplasm as the fourth leading cause of cancer associated with thrombosis (after pancreatic, brain, and lung cancer)

with an incidence rate of 40/1000 person-years. Even within hematological cancers, thrombotic risk varies from one subtype to another. Multiple myeloma and aggressive lymphomas have been reported to have a relative higher risk than the indolent lymphomas and acute leukemia.^[9] For instance, in multiple myeloma in addition to other genetic and acquired risk factors, immobility occasioned by bone pains, cord compression, and pathological fractures associated with the disease further increases the risk of thrombosis. Therapeutic agents used in the management of

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multiple myeloma (e.g., immunomodulators: thalidomide and lenalidomide) are associated with an increased risk of thrombosis which is further worsened when used in combination with steroids and other chemotherapeutics.^[10]

Thromboprophylaxis is the use of anticoagulant therapy in the prevention of a thrombotic event. This practice has been reported to improve the prognosis and quality of life of patients with neoplasm, though with attendant risk of bleeding.^[11,12] Thromboprophylaxis in hemato-oncology is quite challenging, especially in thrombocytopenic patients who have increased risk of bleeding.^[11] Despite the high risk of thrombotic events in patients with hematologic cancers, there is no clear recommendations on the practice of thromboprophylaxis with the exception of multiple myeloma. Randomized clinical trials are needed to establish the best practice for prevention and treatment of VTE in patients with hematologic cancers.^[7]

Study significance

Thromboprophylaxis is the use of anticoagulant therapy in the prevention of thrombotic event. This practice has been reported to improve the prognosis and quality of life of patients with neoplasia including hematologic cancers, though with attendant risk of bleeding. Thromboprophylaxis is recommended in patients with hematologic oncologies,^[13] especially in high-risk patients which include inpatients and multiple myeloma patients on immunomodulatory therapy. Its perception and practice have not been evaluated in our environment. This study seeks to evaluate the perception and practice of thromboprophylaxis in patients with hematological cancers and to identify challenges with the practice of thromboprophylaxis among Nigerian hematologists.

SUBJECTS AND METHODS

This was a questionnaire-based cross-sectional descriptive national study conducted during the 42nd Annual General Meeting of the Nigerian Society of Haematology and Blood Transfusion (NSHBT) held in Lagos October 2016. The NSHBT is an association of professionals who specialize in hematology. It comprises mainly of doctors and laboratory scientists. The questionnaires were self-administered to only doctors including consultants and resident doctors in different cadre of training who gave consent. Doctors who were not hematologists or undergoing specialty training in hematology at the time of the study were excluded.

A 12-item pretested (see Appendix 1) containing questions on the respondents’ sociodemographic characteristics (item 1–3), questions on awareness and practice of thromboprophylaxis in cancer management (item 4, 5, and 6), type of hematological neoplasm they give thromboprophylaxis, choice of agent, and determinants of choice (item 7, 8, and 9, respectively), and facilities available for diagnosis or monitoring of VTE patients (items 10 and 11) as well as challenges encountered in management of patients with VTE was administered to consenting hematologist in attendance.

The data were analyzed with the statistical package for social sciences (SPSS) version 21.0. (IBM corp. Armonk, NY, USA). The responses were expressed as frequencies and presented in tables.

RESULTS

Fifty-five hematologists comprising 31 (56.4%) consultants, 4 (7.3%) senior registrars, and 20 (36.4%) registrars participated in the study. Table 1 shows the institution of origin and duration of practicing hematology by the respondents.

Fifty-three (96.4%) of the respondents were aware of thromboprophylaxis in cancer patients, and 51 (92.7%) practice thromboprophylaxis in their patients with hematological cancers. Table 2 shows the hematological neoplasms for which the respondents use thromboprophylaxis, their preferred agents, and determinants of their choice of thromboprophylaxis. Multiple myeloma is the hematological neoplasm for which most hematologists administered thromboprophylaxis as reported by 46 (83.6%) respondents. The leading choices of thromboprophylactic agent included warfarin, low molecular weight heparin, and low dose aspirin by 33 (60.0%), 25 (45.5%), and 24 (43.6%) respondents. Established guidelines and cost were the major determinants of choice of thromboprophylaxis.

The most accessible diagnostic tool was Doppler ultrasound reported by 51 (92.7%) of respondents. D dimer and angiography were accessible to 28 (50.9%) and 13 (23.6%) of respondents. Prothrombin time and activated partial thromboplastin time were available to 52 (94.5%).

The major challenges to management of patients with VTE as shown in Table 3 included lack of funds to pay for investigations and procure medications, patients’ poor compliance to treatment, and limited capacity of some institutions to investigate the patients due to lack or nonfunctional laboratory

Table 1: General characteristics of the respondents

General characteristics of the respondents	n (%)
Distribution of respondent	
Federal teaching hospitals	33 (60.0)
Federal medical centers	8 (14.5)
State teaching hospitals	10 (18.2)
Private university teaching hospital	2 (3.6)
General hospitals	2 (3.6)
Cadre of hematologist	
Consultants	31 (56.4)
Senior registrars	4 (7.3)
Registrars	20 (36.4)
Duration of practice (years)	
<2	2 (3.6)
2-5	14 (25.5)
5-10	32 (58.2)
>10	7 (12.7)

Table 2: Hematological neoplasms for which respondents do thromboprophylaxis, choice of agent, and determinants of choice

	<i>n</i> (%)
Hematologic malignancies for which they use thromboprophylaxis*	
Multiple myeloma	46 (83.6)
Myeloproliferative neoplasm	17 (30.9)
Chronic myeloid leukemia	15 (27.3)
Chronic lymphoid leukemia	8 (14.5)
Non-Hodgkin's lymphoma	8 (14.5)
Hodgkin's lymphoma	5 (9.1)
Choice of thromboprophylactic agent*	
Warfarin	33 (60.0)
LMWH	25 (45.5)
Low-dose aspirin	24 (43.6)
Dabigatran	9 (16.4)
Rivaroxaban	7 (12.7)
Fondaparinux	3 (5.5)
UFH	2 (3.6)
Elastic stockings	9 (16.4)
What informs choice of agent*	
Established guidelines	38 (69.1)
Cost	29 (52.7)
Availability	23 (41.8)
Minimal risk of bleeding	18 (32.7)
Do not require monitoring	18 (32.7)

*Multiple responses. LMWH: Low-molecular-weight heparin, UFH: Unfractionated heparin

Table 3: Available diagnostic/monitoring tools and challenges of managing patients with venous thromboembolism

	<i>n</i> (%)
Availability of VTE diagnostic/monitoring tools	
Doppler ultrasound	51 (92.7)
Angiography	13 (23.6)
D-dimer	28 (50.9)
PT/APTT test	52 (94.5)
Challenges in managing VTE	
Lack of funds	41 (74.5)
Laboratory insufficiency	20 (36.4)
Noncompliance	28 (50.9)
Difficulties in drug monitoring/drug interaction	2 (3.6)
Availability of drugs/substandard drugs	2 (3.6)
Loss patient to follow-up	1 (1.8)

VTE: Venous thromboembolism, PT: Prothrombin time, APTT: Activated partial thromboplastin time

equipment (laboratory insufficiency) reported by 41 (74.5%), 28 (50.9%), and 20 (36.4%), respectively.

DISCUSSION

Major advancement in the diagnosis and management of patients with hematologic cancers have resulted in increased patient survival; however, the burden of cancer-associated thrombosis

is expected to increase. Therefore, thromboprophylaxis is becoming an important component of care for cancer patients. In the index study, the respondents reported a high level of awareness (96.4%) of thromboprophylaxis in patients with hematologic cancers. Ekwere *et al.*^[14] and Omunakwe *et al.*^[15] in their studies among physicians in tertiary health institutions in Nigeria reported an awareness rate of thromboprophylaxis in cancer of 91.8% and 89.4%, respectively. The rate reported in the index study was higher most probably because the study individuals were specialists in a field that manages hematological malignancies. Respondents in this study being hematologists are quite comfortable with anticoagulation protocols, and this may explain their higher awareness ratings.

We also observed a high rate (92.7%) of practice of thromboprophylaxis in cancer patients. This is significantly higher than the 39.4% reported by Omunakwe *et al.* in their study.^[15] Despite a high level of awareness, the fear of bleeding by physicians has limited their disposition to use anticoagulation, especially in cancer patients whose risk appear higher than in the general populace and noncancer patients.^[16] It is not surprising that hematologists whose specialty also involves management of bleeding have a high rate of use of anticoagulation to prevent thrombosis in cancer patients. This is because they have the capacity to monitor anticoagulation therapy, detect bleeding early, and initiate appropriate measures to control it. It may also depict knowledge gap between the hematology team and the other physicians in the hospital with regards to anticoagulant use and may underscore the need for further medical education in this field.

In the index study, 83.6% of the respondents prescribe thromboprophylaxis for multiple myeloma patients while < one-third administers thromboprophylaxis for other hematological cancers.

Warfarin, low-molecular-weight heparin, and low-dose aspirin in order of decreasing preference were the most prescribed agents by hematologists. A low proportion of the respondents use the novel oral anticoagulants. Despite the fact that warfarin requires regular monitoring and the challenges of achieving target International Normalized Ratio (INR) due to its interaction with drugs and food, it is still the most preferred thromboprophylactic agent. Their preference may be because of its relatively cheaper cost as they report cost (52.7%) as a major determinant of choice while using established guidelines in management of their patients.

Majority (92.7%) reported having access to a Doppler ultrasound which is a very important tool for diagnosis and monitoring of patients. However, just about 50% of them have access to the basic screening tool for D-dimer assay, to exclude patients who may not have thrombosis. The implication is that there is a tendency to depend on doppler, a relatively more expensive test, to evaluate thrombotic risk. This will result to injudicious use of relatively scarce resources. There is need to focus on increasing the capacity of the institutional laboratories to evaluate, diagnose and monitor thrombotic risks through the

use of cost effective laboratory assays. This requires further investigation as a little more funding may increase the capacity of the institutional laboratories to diagnose and manage these cases better. Majority of the respondents have access to basic coagulation screening test (prothrombin time/INR) making it possible to effectively monitor their patients on warfarin.

Scarcity of funds and laboratory insufficiency were identified as the major challenges to effective management of patients. Although there is a National Health Insurance Scheme in Nigeria, the coverage is very low.^[17] Even for those who have access, the scope of care it covers is still limited such that the cost of care is borne mainly by the patients and their relatives. Patients have challenges procuring their anticancer drugs, and any further additional cost arising from the prescription of more medications or investigations further increases their financial stress. This may have prompted their preference for warfarin in this study as it is relatively more affordable when compared to other anticoagulants. As for laboratory insufficiency, although the basic equipment and tests were available to a majority of the hematologists, there is need to improve on the capacity and performance through participation in external quality control programs.

CONCLUSION

Nigerian hemato-oncologists have a good perception and high use of thromboprophylaxis in patients with hematological malignancies, especially multiple myeloma. Warfarin is the preferred anticoagulant because of its affordability.

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Conflicts of interest

There are no conflicts of interest.

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APPENDIX

Appendix 1 (Questionnaire)

Dear Colleague, we solicit your cooperation to evaluate the level of awareness and practice of thromboprophylaxis in patients with hematologic cancers in Nigeria by hematologist. Thank you in anticipation.

1. Name of institution
2. Cadre of doctor:
Medical Officer () Registrar () Senior Registrar () Consultant ()
3. Duration of practice in hematology specialty:
<2 years () 2–5 years () 5–10 years () >10 years ()
4. Are you aware of thromboprophylaxis in cancer patients?
Yes () No ()
5. Do you use thromboprophylaxis for your patients with hematological cancers?
Yes () No ()
6. If no state reasons:
I do not consider venous thromboembolism a problem in them () Not aware of guidelines on thromboprophylaxis () Fear of associated risk () No evidence it is beneficial () Venous thromboembolism is not clinically obvious () Others – Specify (multiple responses allowed)
7. If yes to Q4, for which of these do you administer thromboprophylaxis?
Acute leukemia () CML () Chronic lymphoid leukemia () Multiple myeloma () NHL () HL () MPN () multiple response allowed
8. What is your choice thromboprophylactic agent?
Low-dose aspirin () Warfarin () Low-molecular-weight heparin () Unfractionated heparin () Dabigatran () Rivaroxaban () Fondaparinux () Elastic Stockings () Others (Specify) Multiple response allowed
9. What informs your choice of thromboprophylactic agent?
Established guideline () Cost of agent () Associated risk is minimal () Do not require monitoring () Availability () Multiple response allowed
10. What diagnostic methods are available for venous thromboembolisms in your center?
Doppler Ultrasonography () Angiography () etc.
11. What laboratory tests can be done in your center for monitoring anticoagulation?
Prothrombin time () Activated partial thromboplastin time () D-Dimers () Factor assay ()
12. What problems do you encounter in managing venous thromboembolism patients?
Lack of funds () Laboratory insufficiency () Noncompliance () etc.