Original Article

Challenges in the Management of Bleeding Disorders in Nigeria

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Abstract

Background: Bleeding disorders (BDs) are characterized by abnormal bleeding for which effective management requires a combination of skill, workforce, diagnostic facilities, and adequate therapeutic options. **Objectives:** The objectives of this study were to determine the capacity of Nigerian hematologists to handle BDs and to assess availability of required infrastructure, equipment, and treatment options. **Materials and Methods:** This descriptive study was conducted during the 2016 scientific conference of the Nigerian Society for Hemetology and Blood Transfusion. A structured questionnaire was distributed to hematologists in attendance. Data were analyzed with SPSS version 21. **Results:** A total of 55 (76.4%) hematologists from 27 centers responded. The most frequently carried out tests to assess bleeding were hemoglobin or packed cell volume (100%), full blood count (96.3%), and prothrombin time/international normalized ratio and activated partial thromboplastin time (77%). Many centers did not have a coagulometer (47.8%) or cold centrifuge (43.4%) and none had thromboelastography or rotational thromboelastometry. Fresh whole blood was the most accessible (88.5%) and up to one-third of the centers did not have access to component therapy. Only 39.1% centers had factor concentrates available. **Conclusion:** Facilities required for diagnosing and treating BD are significantly deficient in most centers in Nigeria. Funding to provide facility and training is required to improve on this inadequacy.

Keywords: *Bleeding, hemophilia, thrombocytopenia, whole blood*

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Introduction

Bleeding disorders (BDs) are characterized by prolonged or abnormal bleeding due to disorders of blood vessels, platelets, or coagulation factors. They are sometimes referred to as clotting abnormalities or coagulopathies by different practitioners. The prevalence of BD is variable depending on the population being studied, while the prevalence is about 29%–47% in women presenting with menorrhagia.[1,2] von Willebrand disease (VWD) is thought to be the most common inherited BD affecting 1% of the general population.[3] Acquired BDs are more common than inherited BDs and are usually secondary to multiple coagulation defects.[4] These disorders could be inherited or acquired. BDs are also classified based on the mechanism of defect.

The inherited BDs are grouped into disorders due to coagulation factor deficiency, platelet and fibrinolytic disorders, and vascular and connective tissue disorders. The most common inherited coagulation disorders include hemophilia A (factor VIII deficiency), hemophilia B (factor IX deficiency), factor XI deficiency, and VWD.[5,6] Acquired causes of BD include those resulting from thrombocytopenia (which could be immune mediated, drug induced, or due to hematological malignancies) or disseminated intravascular coagulation (DIC), liver and renal diseases, acquired antibodies against clotting factors, and Vitamin K deficiency, among others.

Patients with BD can present with a myriad of symptoms ranging from mucocutaneous bleeding as

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seen in platelet disorders such as thrombocytopenia or VWD to hemarthroses, hematuria, intramuscular, intracerebral, and retroperitoneal hemorrhages seen in severe hemophilias A and B, severe VWD, and severe deficiency of factors VII, X, and XIII. Spontaneous bleeding, postcircumcision bleeding, and injury-related bleeding can also occur.[3] In addition, menorrhagia could be the first and only symptom of a patient with BD. Given the spectrum of presentation, the different departments or specialties could be the portal of entry for these patients. Furthermore, some may have presented for other medical or surgical problems and the BD detected during examination and laboratory investigations.

A detailed history taking and physical examination as well as basic and readily available investigations is essential in making a diagnosis of BDs. Management of BDs is laden with numerous challenges, which include lack of adequate health-care facilities, low awareness among medical practitioners, lack of multidisciplinary team approach, insufficient number of specialists and specialist centers, lack of effective medical insurance, lack of factor concentrates as seen in hemophilias, insufficient government funding, disease underregistration, and lack of availability of treatment products.[7-9] A study carried out in northern part of Nigeria stated that one of the problems facing the Nigerian health system is limited access to health facilities and that most hospitals in Nigeria are privately owned by individuals and religious organizations which may lack adequate physical structures and equipment, adequate and skilled workforce, and service delivery in general.[10] Reding and Cooper[11] pointed out that barriers to effective diagnosis and management of a BD are due to lapses in knowledge and practice which could be improved by more effective education.

This study aims to determine the capacity of doctors working in hematology units to handle BDs in Nigerian health institutions and also to determine the degree of availability of infrastructure, equipment, and treatment options required for its management.

Materials and Methods

This was a descriptive study conducted in Nigeria during the annual scientific conference of the Nigerian Society for Haematology and Blood Transfusion which held in October 2016.

A structured questionnaire was distributed to hematologists who were in attendance at the conference and practicing in Nigerian institutions involved in the management of BDs. Information including name of institution, number of hematologists present, the availability and functionality of infrastructure and equipment, available investigations, and treatment options necessary in handling BD were sought for. On completion, these questionnaires were retrieved and data were analyzed using the Statistical Package for the Social Sciences (SPSS) software Version 21 (IBM, Chicago, Illinois, USA). Results were presented in tables and as frequencies and percentages.

Results

From the 72 hematologists who attended the meeting, 55 responded giving a response rate of 76.4%. These 55 hematologists were from 27 Nigerian health institutions. Hematologists were involved in patients' management in the clinical departments of all institutions; however, hematologists in only 21 (77.8%) institutions consulted pediatric patients [Table 1].

The most common laboratory section available for work was the general hematology laboratory present in 25 (92.6%) out of the 27 centers. This was closely followed by the coagulation laboratory and blood bank available in 88.9% of the centers. The least available laboratory sections were the research laboratory (51.9%) followed by the residents' laboratories (59.3%), as shown in Table 1.

Hemoglobin (Hb) concentration and packed cell volume were the most frequently carried out investigations (100%). This was closely followed by the full blood count (including platelet count), both equally carried out in 26 (96.3%) centers. Prothrombin time (PT)/international normalized ratio (INR) and activated partial thromboplastin time (APTT) were the coagulation tests frequently carried out in twenty (77%) institutions.

Table 1: Coverage of services and laboratory space

	Total *n* (%)
Wards	
Hematology	24 (88.9)
Medical	24 (88.9)
Pediatrics	21 (77.8)
Obstetrics and gynecology	24 (88.9)
Accident and emergency	24 (88.9)
Others	26 (96.3)
Clinics	
Adult hematology	25 (92.6)
Pediatric hematology	11 (40.7)
Laboratory	
Side laboratories	22 (81.5)
General hematology	25 (92.6)
Coagulation	24 (88.9)
Blood bank	24 (88.9)
Research laboratory	14 (51.9)
Residents' laboratory	16 (59.3)

Table 2: Investigations carried out

Investigations carried out	Frequently, *n* (%)	Occasionally, *n* (%)	Sparingly, *n* (%)	Never, *n* (%)
Hb, PCV	27 (100)	-	-	-
FBC	26 (96.3)	-	1 (3.7)	-
Platelet count	26 (96.3)	-	1 (3.7)	-
Bleeding time	9 (34.6)	9 (34.6)	7 (26.9)	1 (3.8)
Prothrombin time/INR	20 (76.9)	3 (10.8)	2 (7.7)	1 (3.8)
Activated partial thromboplastin time	20 (76.9)	2 (7.7)	1 (3.8)	3 (11.5)
Fibrinogen assay	-	3 (12.0)	7 (28)	15 (60.0)
Mixing studies	1 (4.3)	9 (39.1)	2 (8.7)	11 (47.8)
Hess (Rumple–Leede) test	-	2 (8.6)	3 (913)	18 (76.9)
Factor assay	-	5 (20.9)	5 (20.9)	14 (58.3)
Inhibitor assay	-	3 (12.5)	3 (12.5)	18 (75)
VWF assay	-	1 (4.2)	2 (8.4)	11 (87.5)
Platelet aggregation	-	-	3 (12.5)	11 (87.5)
Platelet factor 4 assay	-	-	3 (12)	22 (88.0)
Fibrinogen degradation products	2 (8.3)	1 (4.2)	6 (25)	15 (62.5)
DNA-based analysis	-	2 (8.3)	1 (4.0)	22 (88.0)

Hb=Hemoglobin; PCV=Packed cell volume; FBC=Full blood count; INR=International normalized ratio; VWF=von Willebrand factor; DNA=Deoxyribonucleic acid

Table 3: Available equipment

Available equipment	Always in use, *n* (%)	Occasionally in use, *n* (%)	Never in use, *n* (%)	Not available, *n* (%)
FBC autoanalyzer	24 (88.9)	1 (3.7)	1 (3.7)	1 (3.7)
Coagulation autoanalyzer	6 (26.0)	5 (21.7)	1 (4.3)	11 (47.8)
Microhematocrit centrifuge	25 (100)	-	-	-
Water bath/incubator	23 (88.4)	1 (3.8)	0	2 (7.6)
Coagulometer	8 (34.8)	2 (8.7)	2 (8.6)	11 (47.8)
Multiplate	-	1 (5.3)	1 (5.3)	16 (84.2)
Cold centrifuge	8 (34.8)	3 (13.0)	2 (8.7)	10 (43.4)
Apheresis machine	4 (16.70)	4 (16.7)	3 (12.5)	12 (50)
TEG	-	-	-	23 (100)
ROTEM	-	-	-	23 (100)
PCR	-	2 (9.5)	4 (19.1)	15 (71.4)

FBC=Full blood count; TEG=Thromboelastography; ROTEM=Rotational thromboelastometry; PCR=Polymerase chain reaction

Table 4: Treatment options

Access to therapeutic options	Always, *n* (%)	Occasionally, *n* (%)	Never, *n* (%)
FWB	23 (88.5)	2 (7.7)	1 (3.8)
Packed red cells	20 (80.0)	5 (20.0)	-
Apheresis platelet concentrates	8 (33.3)	6 (25.0)	9 (37.5)
Platelet-rich plasma	8 (34.8)	5 (21.7)	7 (43.4)
Fresh frozen plasma	7 (31.8)	7 (21.8)	8 (36.4)
Factor VIII concentrate	4 (17.4)	5 (21.7)	14 (60)
Factor IX concentrate	3 (13.0)	5 (21.7)	15 (65.3)
Factor VIIa	1 (4.5)	1 (4.5)	20 (90.9)
Cryoprecipitate	3 (13.6)	3 (13.6)	15 (68.2)
Prothrombin complex concentrate	2 (9.1)	-	20 (90.9)
Vitamin K	6 (66.6)	4 (16.7)	4 (16.7)
Desmopressin	11 (50)	7 (31.8)	42 (18.2)
Tranexamic acid	12 (48.0)	11 (44.0)	2 (8.0)
Steroids	22 (88.0)	2 (8.0)	1 (4.0)
Fibrin glue	1 (4.3)	1 (4.3)	20 (86.9)

FWB=Fresh whole blood

Most of the other coagulation investigations were not carried out in those centers. Majority of the institutions did not carry out Hess/Rumple–Leede test (76.9%), inhibitor assay (75%), fibrinogen assay (60%), factor assay (58.3%), and mixing studies (47.8%). von Willebrand factor assay was only sparingly done in two (8.4%) centers. DNA-based tests were never carried out in 22 (88%) institutions as summarized in Table 2.

Of the available equipment, microhematocrit centrifuge was the most used (100%) followed by the full blood count auto-analyzer, 24 (88.9%). None of the respondents had thromboelastography or rotational thromboelastometry in their centers, while most centers did not have multiplate (84.2%), polymerase chain reaction (PCR) machine (71.4%), apheresis machine (50%), coagulometer (47.8%), and cold centrifuge (43.4%). The PCR, apheresis, and ELISA machines were present but had never been in use in 19.1%, 12.5%, and 8.3% of the institutions, respectively [Table 3].

Fresh whole blood was the most accessible therapeutic option in 23 (88.5%) institutions; others were packed red cells, steroids, heparin, and Vitamin K available in 20 (80%), 22 (88%), 19 (76%), and 14 (46.6%) institutions, respectively. Of the institutions under study, 20 (90.9), 20 (86.7%), and 15 (65.2%) of them stated that FVIIa, fibrin glue, and FIX, respectively, were never available as treatment options. Only nine (39.1%) centers had FVIII available [Table 4].

In the past 1 year, DIC was the most encountered BD in these centers followed by hemophilia with 214 and 164 cases, respectively. Cases of immune thrombocytopenic purpura (ITP), other acquired platelet disorders, inherited platelet disorder, and vasculopathy were handled 97, 43, 11, and 9 times, respectively. Hematologists in 12 (41.4%) of the institutions have had a formal training on the management of BD in the past year, the same number agreed not to have had any training. Majority of the hematologists, 25 (92.6%), in the centers under study believe they would benefit from such training.

Discussion

This survey includes information on hematology services across all geopolitical zones in the country. There was a good response rate, with response from more than three quarters of the hematologists who attended the meeting.

Bleeding diathesis occurs as a frequent hematological emergency and the capability of a center to handle this feature may have an important association with mortality and prolonged hospital stay. We found that majority of the centers studied had general hematology and coagulation laboratory spaces; however, while all centers performed full blood count (thereby being able to assess the platelet count and Hb), only about three-quarters of them offered the basic coagulation screening tests (PT/INR and APTT). This portrays a disability in diagnostic protocol in these disadvantaged centers and implies a consequent shortfall in the clinical management of bleeding patients in such settings.

Second-line investigative tests were largely unavailable in more than half of the centers. This showcases the fact that majority of the tertiary health facilities in the different parts of the country are ill equipped to make a diagnosis of BDs. From this study, we observed that despite having few centers where factor assay can be done for the diagnosis, treatment, and monitoring of hemophilia, many hemophiliacs are being followed up in these centers. This may reflect the effective referral system in place where suspected cases are sent to centers capable of making the diagnosis after which the patients are referred back to their primary/home centers for treatment and follow-up. However, this may impact negatively on outcome as some emergency cases may require some facilities to make prompt diagnosis not available in their home centers.

Therapeutic management of bleeding irrespective of the underlying cause requires the availability of an efficient blood transfusion service with easy accessibility of blood and blood products. In our study, whole blood was available in majority of the centers investigated; however, approximately half of them lacked the capacity to produce blood components. The practice of whole-blood transfusion is wasteful and exposes patients to unnecessary immunological and nonimmunological challenges. According to the World Health Organization, only 43% of blood collected in low-income countries is separated into components, compared to 78% and 96% in middle- and high-income countries, respectively.[12] Not all cases of bleeding due to thrombocytopenia may require platelet concentrate, such as in thrombocytopenia from immune-mediated causes or thrombotic thrombocytopenic purpura. However, in most other causes of bleeding due to severe thrombocytopenia from conditions such as hematologic malignancies, aplastic anemia, DIC, or as a side effect of chemotherapy, platelet concentrate transfusions are essential.[13] Platelet concentrates may also be useful in cases of platelet dysfunction or prophylactically in patients who have a high risk of bleeding. In the Western world, transfusion of most platelet concentrates was done prophylactically to reduce the risk of bleeding.[14] Platelet concentrates are only available in 15 of the 27 centers. In addition, they are costly (220USD about 3 years ago)[15] and have to be paid for by the patient, which strongly limits their use. It is, therefore, unfortunate that component therapy is not yet widespread in Nigeria and this will impact negatively on the outcome of severely thrombocytopenic patients, especially those who present with major bleeding. Just like platelet concentrates, other blood components such as fresh frozen plasma and cryoprecipitate were not readily available in most centers, also reflecting the few numbers of refrigerated centrifuges and apheresis machine available as observed in this study.

More than 60% of the centers had no access to factor concentrates or fibrin glue. This casts a dull shadow in the management of hemophiliacs in such settings and implies that whole blood is usually given with consequent suboptimal factor replacement in a background of fluid overload and allo-immunization. A survey by the World Federation of Haemophilia in 2006 showed that Nigeria had a mean factor use per capita of 0.002, compared to South Africa at 0.832 and the United States at 5.16.[16] The most commonly

encountered BDs in clinical practice are the acquired BDs, with DIC being one of the most common types. Bleeding is the most readily apparent clinical feature of DIC. These may explain why respondents reported to have encountered DIC most in their practice and being one of the most common acquired BDs.[17] As a result, whole blood (in the absence of component therapy) and tranexamic acid were seen as the most commonly available treatment options in this study. At the same time, 88% of respondents accepted to frequently use steroids, the first-line treatment for ITP, which is equally one of the common acquired BDs.

This study also shows that less than half of the participants had had a formal training in the field of hemostasis in the previous year, thereby impacting negatively on the care of patients with BDs. Although continuous medical education (CME) is required by the Nigerian Medical Association before annual renewal of doctors' practicing license, it does not specify the specialty areas for doctors. Therefore, hematologists may have received CMEs in some other aspect of hematology, excluding the field of hemostasis.

The establishment of basic minimum tests, equipment, treatment options, and personnel training for effective management of patients with BDs in these institutions is necessary. These include tests such as full blood count, bleeding time, PT/INR, APTT, thrombin time and fibrinogen assay, equipment to produce blood components, and other treatment options such as the factor concentrates.

Conclusion

There is significant deficiency in most centers in Nigeria to adequately diagnose the underlying cause in a bleeding patient. Therapeutic options are also limited to whole-blood transfusion and tranexamic acid as there is poor access to component therapy or clotting factor concentrates. This study reveals some of the challenges in the care of patients with BDs in a resource-poor setting.

Recommendations

Massive funding is required for major Nigerian health institutions in order to provide infrastructure, facility, and training required in the diagnosis and treatment of patients who present with BDs.

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Conflicts of interest

There are no conflicts of interest.

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