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Application of the ISTH bleeding score in hemophilia

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ABSTRACT

Background: Hemophilia is an inherited bleeding disorder. With proper treatment and self-care, persons with hemophilia can maintain an active, productive lifestyle. Hemophilia can be mild, moderate, or severe, depending on the degree of plasma clotting factor deficiency. The aim of the study was to assess the utility of ISTH-BAT in diagnosis, determining severity of the bleeding condition in newly diagnosed and known hemophilia patients, compare the bleeding score (BS) in adult and pediatric groups and investigate its association with plasma factor levels.

Methods: ISTH-BAT was used to assess BS in a total of 115 patients, 78 with hemophilia A, and 37 with hemophilia B and in 100 controls.

Results: BS was significantly higher in HA and HB patients as compared to controls, with no significant difference between HA and HB. The BS was very similar in newly diagnosed compared to known hemophilia patients, lower in pediatric compared to adult and higher in severe compared to mild HA patients.

Conclusion: The ISTH BAT can help identify hemophilia patients. Therefore it is a useful tool to distinguish between affected and unaffected individuals with bleeding. Moreover, an important finding of our study is that there is no major difference between the scores in known and newly diagnosed patients.

1. Introduction

Hemophilia is an inherited bleeding disorder. With proper treatment and self-care, persons with hemophilia can maintain an active, productive lifestyle. The disease results from a genetic defect in the X-chromosome and affects mainly males. Hemophilia is classified based on the deficiency of type of clotting factor, deficiency of factor VIII in type A hemophilia (HA) and deficiency of factor IX in type B hemophilia (HB) can be mild, moderate, or severe, depending on the degree of plasma clotting factor deficiency. The symptoms include many large or deep bruises, joint pain and swelling caused by internal bleeding, unexplained and excessive bleeding, blood in urine or stool, nosebleeds, prolonged bleeding from cuts or injuries or after surgery and tooth extraction [1–3].

Evaluating the presence and severity of bleeding symptoms is a fundamental step in the assessment of patients' clinical outcomes [4]. The ISTH/SSC joint committee established a bleeding assessment tool (BAT), to standardize the reporting of bleeding symptoms [5].The ISTH-BAT scores bleeding symptoms from 0 (absence or trivial symptoms) to 4 (symptom requiring medical interventions) [6]. Limitations of BATs exist, however, in particular for pediatric patients because of a lack of exposure to hemostatic challenges particularly in mild bleeding disorders. To date, the majority of research on bleeding questionnaires has been focused on von Willebrand disease (VWD) and to a lesser extent on platelet disorders with very little if any on hemophilia [7–11].

Several local studies conducted on inherited bleeding disorders have shown that hemophilia A (HA) is the most commonly identified bleeding disorder in our geographic area [12–15]. In contrast to the Western world, hemophilia patients in Pakistan can often not afford regular (prophylactic) treatment with clotting factor concentrates. This cross sectional study aims as a first step to: 1) quantify and compare ISTH-BAT scores in patients with hemophilia (A and B) with healthy controls; 2) within hemophilia patients: a) compare adult and pediatric bleeding scores (BS), b) compare scores between already diagnosed and undiagnosed patients; c) compare scores among mild, moderate, and severe HA and HB; and 3) correlate bleeding scores with factor levels. In developed countries, the diagnosis of hemophilia is usually made during childhood. Due to the limited healthcare resources in Pakistan patients with hemophilia are often only recognized after childhood age. This provided the unique chance to compare the association of the BAT

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Table 1
Demographic characteristics and bleeding scores of hemophilia patients and controls.

Demographic characteristics	Hemophilia A N = 78	Hemophilia B N = 37	Controls N = 100
Age (mean ± SD)	11.8 ± 9.8	18.1 ± 10.2	15.5 ± 8.2
Pediatric group (< 12); **n** (%)	47(60.3)	10(27.0)	
Adult group (≥12); **n** (%)	31(39.7)	27(73.0)	
Factor Level Categories			
Severe; n (%)	34(43.6)	14(37.8)	NA
Moderate;n (%)	37(47.4)	20(54.1)	
Mild; n (%)	7(9)	3(8.1)	
Bleeding scores (BS)			
Mean ± SD	13.5 ± 7.3	13.2 ± 5.3	0.8 ± 1.4
Pediatric group (< 12);(mean ± SD)	12.1 ± 6.4	11.9 ± 5.5	
Adult group (≥12); (mean ± SD)	15.9 ± 8.0	13.8 ± 5.3	
Severe; (mean ± SD)	15.5 ± 8.2	16.0 ± 5.6	None
Moderate; (mean ± SD)	12.4 ± 6.4	12.3 ± 4.1	
Mild; (mean ± SD)	10.4 ± 5.02	6.0 ± 2.0	

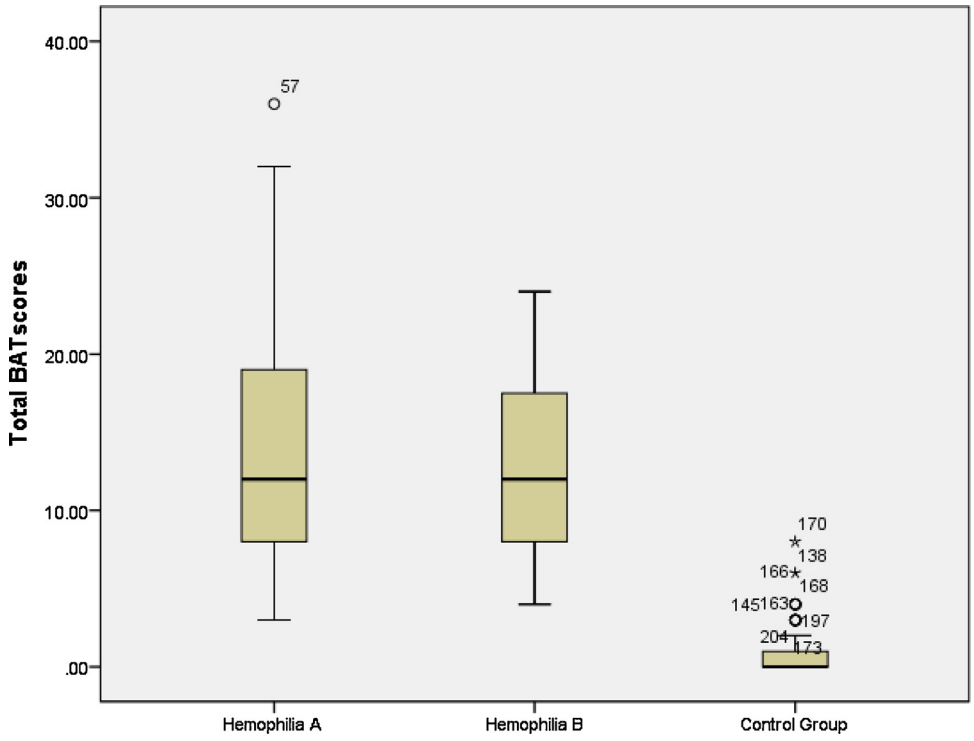

Fig. 1. Comparison of bleeding scores in Hemophilia A, Hemophilia B and Control group.

and factor levels obtained in previously undiagnosed hemophilia patients (before the factor levels became available) with the BAT in known hemophilia patients within the study.

2. Material & methods

This cross sectional study was conducted at the National Institute of Blood Disease & Bone Marrow Transplantation (NIBD), Karachi, Pakistan after getting approval from institutional ethics committee and in accordance with the declaration of Helsinki. Adult (> 12 years) and pediatric (< 12 years) HA and HB patients of various ages and severity were included who visited hospital for inpatient and/or outpatient services from January 2014 to December 2016. Twelve year cut-off was selected as most patients were adolescents and young adults. These patients were divided into 2 groups:previously diagnosed hemophilia patients and new patients with bleeding symptoms before their hemophilia diagnosis. Patients with other bleeding disorder were excluded from the study. One hundred healthy male controls comprised of relatives of patients and blood donors who visited our institute were included in the study. Written informed consent was obtained from all participating subjects (patients and or legal guardians).

Laboratory diagnosis of HA and HB was based on plasma coagulation factor assays (factor VIII, IX and other factors as required) and assays of von Willebrand factor antigen and activity. Clinical evaluation was performed through detailed clinical history and careful assessment of bleeding manifestations which included the type and site of bleeding, presence or absence of joint deformity, number of joints involved, hematoma formation, intra cranial bleeds as well as the duration, type of therapy including any surgical intervention. A team of hematologist and a trained clinical research officer in the outpatient clinics conducted these assessments and administered the ISTH BAT. For the previously diagnosed hemophilia patients, ISTH BAT was administered at their outpatient visit (before on demand treatment) and for new patients ISTH BAT was administered at the time of their initial visit before the diagnosis of hemophilia was established.

BS ≥ 4 in adult males, ≥6 in adult females and ≥3 in children was