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# Evaluation of International Society on Thrombosis and Hemostasis-Bleeding Assessment Tool (ISTH-BAT) scores in hemophilia patients: Single center experience

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## Abstract

**Aim:** We aimed to examine the relationship between the clinical bleeding severity classification based on the factor levels and the ISTH-BAT score (calculated numerically over +/- or 10), to evaluate the usability of the ISTH-BAT score in Hemophilia A and B.

**Materials and Methods:** In this retrospective study, the data of hemophilia A and B patients who were administered a face-to-face ISTH-BAT survey upon admission to the outpatient clinic were evaluated. In addition to the positivity rate of the ISTH BAT score of patients with hemophilia, the relationship between this score and the patient's age, hemophilia type and factor level was also evaluated.

**Results:** The study included 158 male patients (n:125 hemophilia A, n:33 hemophilia B). ISTH-BAT positivity was detected in 45.6% of hemophilia A patients and 57.6% of hemophilia B patients. There were no significant differences between hemophilia A and hemophilia B patients in terms of ISTH-BAT scores (p=0.43). Scores were higher in severe hemophilics, as expected, but there was no statistically significant correlation between factor levels and ISTH-BAT scores in hemophilia A (p=0.56), or hemophilia B (p=0.54).

**Conclusion:** The ISTH-BAT can help recognize individuals with a bleeding history without a diagnosis. However, it does not correlate with factor level in patients with hemophilia and is not effective in determining bleeding susceptibility. Plasma factor levels are the most predictive data for bleeding frequency and severity.



## Introduction

Hemophilia is a hereditary bleeding disorder that is classified based on the deficiency of the clotting factor type, factor VIII in hemophilia and factor IX in B hemophilia [1]. Clinical severity is classified depending on the level of plasma clotting factors as; mild (>5%), moderate (1-5%), or severe (<1%). Bleeding signs and symptoms have the potential to impact all systems. These encompass skin bruising, joint discomfort, and swelling resulting from internal bleeding, epistaxis, as well as bleeding within the gastrointestinal and genitourinary systems, evident as hematemesis, hematochezia, melena, extended bleeding following cuts, injuries, surgeries or tooth extractions, and even critical intracerebral hemorrhages.

Patients with severe hemophilia experience recurrent acute joint bleeding, which can lead to chronic synovitis and joint disability. Roughly 90% of patients experience the onset of chronic hemophilic arthropathy by the age of 30, leading to persistent pain, disability, and impaired health-related quality of life (HRQoL) [2].

Therefore, various bleeding scores have been developed to standardize bleeding severity for objective and quantitative final scores due to difficulties in reporting subjective hemorrhagic symptoms [3]. The International Society on Thrombosis and Hemostasis-Bleeding Assessment Tool (ISTH-BAT) is one of these questionnaires that has been assessed as a pediatric screening tool for individuals with a possible inherited platelet function defect/primary hemostasis [4]. Its use in adult Hemophilia hasn't been validated.

To evaluate the usability of the ISTH-BAT score in

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Hemophilia A and B, we aimed to examine the relationship between the clinical bleeding severity classification based on the factor levels and the ISTH-BAT score (calculated numerically over +/- or 10).

## Materials and Methods

### *Patients*

A total of 158 male patients (125 hemophilia A and 33 hemophilia B) over 18 years who were followed up in Gülhane Educational and Research Hospital Department of Hematology between 2013-2016 were included in this study. Patients were previously diagnosed with hemophilia A or B of various severity and without inhibitors. 2 hemophilia A (n:1 age:38 Anti-Hypertensive, n:1 age 35 Oral Anti Diabetics) and 1 Hemophilia B (n:1 age:42 Coronary artery disease-antiaggregant) patients using drugs for co-morbid disease were excluded from the study. The study was continued with 125 Hemophilia A and 33 Hemophilia B patients.

Ethics committee approval was obtained from the Gülhane Educational and Research Hospital Ethics Committee on 26.06.2018 and numbered 18/197.

### *ISTH-BAT score*

Clinical severity is classified due to plasma coagulation factor activity levels as; mild (>5%), moderate (1-5%), or severe (<1%). The referring physician at outpatient clinics administered the ISTH-BAT questionnaire to each enrolled patient face-to-face. The normal bleeding score (BS) range was accepted as 0–3 in adult males, and 0–5 in adult females due to the merging project. ≥4 bleeding score in adult males, and≥6 in adult females was defined as BAT positive [3].

### *Statistical analysis*

Statistical analyses were performed using the SPSS software version 20. Descriptive statistics were presented as mean, standard deviation, median, minimum value, and maximum value. For the normal distribution of the values obtained from the measurement methods, the differences between the values were performed with Kolmogorov-Smirnov test (≥50 samples) and the Shapiro–Wilk test (<50 samples). In the comparison of the categorical variables, Pearson's chi-squared test was used. In the comparison of the nonparametric variables obtained from the measurement methods, Mann Whitney U test was used. In the comparison of the ordinal variables Kruskal-Wallis test was used. The relationship between the values obtained from the methods was evaluated by Spearman correlation test. The p-value <0.05 was considered significant.

## Results

The mean age was 22.9±2.6 years, with a median of 23 (Min-Max:19-32) years for hemophilia A, and a mean of 22.5±4.6, median of 20 (Min-Max:19-40) years for hemophilia B patients. There was statistically significant difference between age values in hemophilia A and hemophilia B (p=0.02). Age values in hemophilia B were higher than in hemophilia A. All of the patients were male. The patient's prophylaxis status is unknown. The median application time of the questionnaire was 12 minutes (9-18) for each patient. The median BS was 3.0(min:0-max:9) in hemophilia A patients and 4(min:0-max:10) in hemophilia B patients, although individual scores ranged between 0 and 10. There was no statistically significant difference between BS in hemophilia A and in hemophilia B (p:0.43) BAT positivity was detected in 45.6% of hemophilia A and 57.6% of hemophilia B patients. There was no statistically significant difference between hemophilia A and hemophilia B patients in terms of IST-BAT positivity (p=0.30) (Table 1).

**Table 1.** Evaluation of ISTH-BAT score in hemophilia A and B patients.

| | BAT+ | | BAT- | | Total | | P value |
|---|---|---|---|---|---|---|---|
| | n | %* | n | %* | n | %** | |
| Hemophilia A (n=125) | 57 | 45.6 | 68 | 54.4 | 125 | 79.1 | 0.30 |
| Hemophilia B (n= 33) | 19 | 57.6 | 14 | 42.4 | 33 | 20.9 | |

≥4 bleeding score in adult males, ≥6 in adult females was defined as BAT positive
Pearson's chi-squared test *: row % **: column %.

**Table 2.** Evaluation of ISTH-BAT scores according to severity in hemophilia A and hemophilia B patients.

| | Hemophilia A (n=125) | | | Hemophilia B (n= 33) | | |
|---|---|---|---|---|---|---|
| Severity | n | ISTH-BAT score median(min;maks) | p | n | ISTH-BAT score median(min;maks) | p |
| Severe | 34 | 4(2-7) | | 10 | 2(0-8) | |
| Moderate | 27 | 4(0-7) | 0.75 | 5 | 3(2-4) | 0.05 |
| Mild | 64 | 3(2-4) | | 18 | 4(2-10) | |

Kruskal-Wallis test.

There was no statistically significant difference between severity and ISTH-BAT scores in hemophilia A (p=0.75), or hemophilia B (p=0.05) (Table 2). Although not statistically significant, it was observed that ISTH-BAT scores were higher with increasing disease severity in hemophilia B patients. There was no correlation between activated partial thromboplastin time (aPTT) values and ISTH-BAT scores in hemophilia A and B ( respectively p=0.58, p=0.18). There was no statistically significant difference between activated partial thromboplastin time (aPTT) values in hemophilia A (median(min;max) aPTT: 54.9(32-135.1)) and B (median(min:max) aPTT: 55.6(33.9-109.7) (p:0.75) (Mann Whitney U test). There was a negative correlation between age and ISTH-BAT score in hemophilia A (correlation coefficient: - 0.22, p=0.015) but there was no correlation between age and ISTH-BAT score in hemophilia B (p=0.062).

## Discussion

The development of bleeding assessment tools depends on the need for improved diagnostic accuracy, thus avoiding unwarranted laboratory testing, the identification of objective symptom severity, predicting the risk of future bleeding, and appropriate treatment management [5].

Following the initial publication of the Vicenza Bleeding Questionnaire (BQ) in 2005, multiple successive BATs have been created using the original as a foundation, incorporating modifications intended to enhance both the simplicity of evaluation and the precision of scoring [6]. Assessment of bleeding symptoms is often difficult for physicians and also for patients due to subjective interpretations. In 2010, Rodeghiero et al. published ISTH-BAT based on large participant data to optimize BAT [4]. Crafted for application in both pediatric and adult populations, its aim is to enhance precision by factoring in both the frequency and severity of bleeding episodes. The foremost alteration in the ISTH-BAT scoring mechanism involved the elimination of the -1 score previously assigned for the lack of excessive bleeding subsequent to tooth extraction, surgical procedures, and postpartum situations. The time to administer the questionnaire to the patients is approximately 20 minutes. ISTH-BAT is intended for use in children and adults within a reasonable time of administration, taking into account the frequency (in addition to the severity) of bleeding [4].

Bleeding is the most common symptom in hemophilia patients and may lead to chronic problems such as target joint development, morbidity, loss of labor, and life-threatening bleeding. ISTH-BAT can be used as an indicator for the definition and severity of bleeding in hemophilia patients. It may also contribute to less use of coagulation tests, clinical management of patients and evaluation of treatment efficacy.

Borhany et al. illustrated a striking resemblance in bleeding scores between recently diagnosed and previously recognized hemophilia patients. They emphasized the capability of ISTH-BAT to discern individuals with hemophilia, underscoring its value in distinguishing those experiencing bleeding issues. Notably, their study's significant revelation lies in the absence of a notable contrast in scores between established and newly diagnosed patients [7].

ISTH-BAT was developed for detecting the bleeding disorder in a patient with symptoms and beneficial for avoiding unnecessary laboratory tests and detecting healthy vWD carriers. In our study, we evaluated the already diagnosed hemophilia patients and there was no correlation between ISTH-BAT scores and type of hemophilia, plasma coagulation factor levels, clinical severity, and aPTT values. The negative correlation between age and ISTH-BAT score in hemophilia A can be explained as young patients being more active in school and working life, but there is not an explanation about hemophilia B patients.

In our study, irrespective of the factor types ISTH-BAT scores positivity was evaluated in 54% of hemophilia patients. This rate is actually below the expected rate and suggests that the sensitivity of ISTH-BAT is low. An assessment aimed at identifying preoperative bleeding disorders in patients revealed that ISTH-BAT exhibited noteworthy specificity but relatively limited sensitivity. This suggests that these screening methods might not effectively rule out mild coagulation factor deficiencies, von Willebrand factor irregularities or platelet function impairments. Their investigation indicated that hemostatic irregularities were present in approximately 9%-10% of individuals, regardless of whether they reported bleeding symptoms or not. These outcomes imply that the ISTH-BAT questionnaire might not effectively distinguish between individuals with underlying abnormalities and those without [8].

Evaluation of the bleeding severity is important in clinical course and follow-up, in acute and long-term morbidities and plays a role in the quality of life. We detected that ISTH-BAT is not effective in predicting bleeding risk in hemophilia patients. Plasma factor level is more realistic data for predicting bleeding risk in hemophilia patients.

It made statistical analysis difficult due to the low number of patients in general. Secondly, less common factor deficiencies such as Factor VII and Factor XI deficiencies were not included in the study because a sufficient number of patients could not be reached. Due to the lack of data on the use of prophylaxis treatment by the patients, we could not evaluate those who received and did not receive prophylaxis as a subgroup in the statistical analysis.

## Conclusion

Application of health-related quality-of-life questionnaires for hemophilia and revised bleeding scoring systems together can give an idea about the severity of bleeding, loss of labor, development of target joints and difficulties in the lives of hemophiliacs in cases where factor levels cannot be detected. However, laboratory evaluation is recommended in clinically suspected cases due to its low sensitivity alone.

### *Ethical approval*

Ethics committee approval was obtained from the Gülhane Educational and Research Hospital Ethics Committee on 26.06.2018 and numbered 18/197.

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