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# Comparative Analysis of Bleeding Frequency and Factor Utilization in Severe Hemophilia A and Hemophilia B Patients: Implications for Clinical Phenotype Variability

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**Abstract**
In haemophilia A and B, blood coagulants are reduced because of X-linked genetic factors. A study found that severe Haemophilia A (HA) tends to have a higher Hemophilia Severity Score (HSS) than severe Haemophilia B (HB). HA and HB patients were compared in terms of bleeding frequency and factor utilization. The data were collected from the records of our Haemophilia Clinic in a retrospective study conducted within a single institution. Hemophilia A and Haemophilia B were diagnosed in 88 and 16 subjects, respectively. A plasma-derived factor concentrate was administered on-demand to all of the patients. In this study, Chi-square, Man-Whitney U, and one-sample T tests were used. Version 12.1.4 of MedCalc Statistical Software was used for all calculations. Haemophilia A patients were admitted at a rate of 3.125 patients per year, while Haemophilia B patients were admitted at a rate of 0.77 patients per year (P 0.05). For haemophilia A patients, 3731500IU of FVIII (21201.704IU/patient/year) was used, whereas for haemophilia B patients, 611000IU of Factor IX (17457.142IU/patient/year) was used. The factor concentrations did not differ statistically significantly (P = 0.57). This study suggests Hemophilia A and Hemophilia B are inherited coagulation disorders that are clinically distinctive that differs depending on the severity of the disease. A recent study similar to ours also found results that are in agreement with ours.
**Keywords**: Hemophilia A, Factor Concentration, Hemophilia B, Utilization Evaluation

## Introduction

A common misconception is that A hemophilia B (HB) is the same as a hemophilia A (HA) clinical manifestations, and their clotting activities cannot be distinguished without assessing IX and VIII play specific roles [1]. Generally, hemophilia is diagnosed based on the difference in Level of coagulation correlates with bleeding type factors VIII and IX activity. Biggs and MacFarlane's original hemophilia classification and Thrombotic Society International and Homeostasis standard classification are both widely accepted as valid [2]. However, there is some evidence that the severity of HA and HB may have different bleeding tendencies. Recent studies have suggested that Factor consumption is higher in HA patients because bleeding is more prevalent is greater in HA than in HB even when plasma factor levels are similar [3]. Further, hemophilia severity had to be assessed in order to validate a composite score. Despite similar levels of plasma factor deficiency, the severity of HA was found to be greater than that of HB [4]. Joint arthroplasty is three times more likely to be performed on HA patients than on HB patients of the same severity. In order to compare HA with HB patients, it would have been better to assess the frequency of bleeding since joint arthroplasty indicates an indication of the disease's severity [5]. When patients are on prophylactic treatment, it is difficult to determine how many bleeding episodes there have been. They report every instance of joint pain as bleeding, even if they experience no or limited joint bleeding. On the other hand, patients who receive Hospitals tend to ignore small joint bleedings when patients receive treatment on demand, particularly when they do not receive home treatment. When defining clinical study phenotype scores, this effect should be considered. In haemophiliacs with the same factor activity, bleeding severity and frequency are variable, so approximately 10-15% of haemophiliac patients will experience mild bleeding. In vivo, FIX's initial distribution volume is significantly larger than FVIII's, which is responsible for its lower in vivo recovery, when the recovery of factor concentrations in vivo has been adjusted. Fix binds rapidly to vascular endothelium, explaining this phenomenon. Haemophilia B requires higher initial FIX dosages than haemophilia A due to the fact that FIX is only partially recovered in vivo, therefore the dosage should be adjusted accordingly. As a result, In comparison

to FVIII, FIX has a longer plasma half-life, suggesting an extended interval between doses based on the pharmacokinetic parameters reported by several studies on adults. Comparison of FVIII and FIX consumption patterns and admission rates between HA and HB patients with any level of bleeding tendency.

**Methodology**

We collected the data of all eligible hemophilia patients at our hemophilia treatment center. As part of the confirmation tests, STA performed an assay for FVIII and FIX with a one-stage process. A STA analyzer (Diagnostica Stago, France) was used to perform immune-depleted plasma testing in cases of FVIII and FIX deficiency. An assay using FVIII and FIX inhibitors were detected using the Bethesda method. With different levels of FVIII and FIX deficiency, we examined bleeding and factor consumption in patients. Data was analyzed retrospectively by all electronic medical records of patients treated in one single hospital. Results presented as Mean ± SEM were statistically significant when a $P^*$value of 0.05 was used. The Kolmogorov-Smirnov Analyses were conducted using a test the normal distribution.

**Results**

There was 0.14-15.50 IU/dl of FVIII in 88 HA patients (4.18 x 0.31). In 14 HB patients, the average FIX level was 0.17 to 8.37 IU/dl (2.24 + 2.23). A total of 17 HB patients showed that inhibitor mean levels ranged between 0 and 1.60 BU. The inhibitor titers of Haemorrhagic and hemolytic patients were low in general. According to this study, there were 275 bleeding admissions among 88 HA patients over 12 months compared to 14 bleeding admissions among 16 HB patients (bleeding admission and admission rate are the same term here). Patients with HA experienced 3.125 bleedings per patient year compared to patients with HB who experienced 0.77 bleedings per patient year (P = 0.031). Patients with HA used 3731500 IU of factor content (FVIII) per year (21201.704 IU), and those with HB used 611000 IU of factor content (FIX) per year (17457.142 IU). Using factor concentrations differently did not produce a statistically significant difference (P = 0.570). The tables 1 and 2 provide information about the patients' characteristics.

**Table: 1** A comparison of the differences in haemophilia types based on the concentration of factor concentrates

| **Type** | **Number (104)** | **Age (year)** | **Bleed (Per year)** | $P^*$ |
|---|---|---|---|---|
| Severe Haemophilia | 30 | 31.51 ± 8.80 | 160 | 0.040 |
| Severe Haemophilia | 8 | 25.19 ± 8.01 | 6 | |
| Moderate Haemophilia | 29 | 31.22 ± 10.99 | 91 | 0.028 |
| Moderate Haemophilia | 6 | 28.70 ± 7.76 | - | 0.009 |
| Mild Haemophilia | 27 | 34.04 ± 13.75 | 24 | 0.760 |
| Mild Haemophilia | 4 | 41.21 ± 10.70 | - | 0.005 |

**Table 2:** Comparing hemophilia types A and B based on quantitative parameters

| **Type** | **Number (104)** | **Age (year)** | **Bleed** | | | **Factor concentrates used (IU)** | | |
|---|---|---|---|---|---|---|---|---|
| | | | **Per** | **Patient/ Year** | **P** | **Per** | **Patient/ Year** | **P** |
| Haemophilia A | 88 | 39.30 ± 11.31 | 275 | 3.126 | 0.031 | 1865750 | 10600852 | 0.570 |
| Haemophilia B | 16 | 28.78 ± 10.70 | 13 | 0.771 | - | 305500 | 8728.571 | - |

**Discussion**

Factor concentrates were given to all patients on demand because of the high concentrations found in this study are very expensive and limited in supply; therefore, determining bleeding numbers may be more realistic.

One study revealed that joint arthroplasty risks differ for severe HA and HB despite the fact that these inherited coagulation disorders. According to conventional wisdom, they are identical clinically [6]. Three-fold more patients with HA require arthroplasty, regardless of the location of the prosthesis [7]. It may be due to several reasons that hemophilia types have differing bleeding and admission rates. There are usually fewer null mutations in 12 HB than in HA, as demonstrated by the Italian mutation database. Large deletions, nonsense mutations, and rearrangements mostly cause it.

In spite of the small analysis of 88 HA patients and 16 HB patients was conducted in this study and all of our findings were in agreement with other studies published recently. At all levels of severity, HA admission rates amounted to 2-3 times more than HB admission rates, with little difference between levels of severity, according to a study [8].

Factor concentrate usage in Analogous studies have also been conducted, was not statistically significant. FIX infused into the body recovers more slowly in vivo was attributed to the lower amount of factor concentrate used. It is estimated that, it takes approximately 1 unit of infusion to recover 1 kilogram of weight after an infusion because factor IX has a volume distribution that is twice as large as total plasma volume; however, recombinant factor IX infusions have a 20% lower recovery than plasma derived concentrations. Despite study findings, all patients with mild or severe HB may not need primary prophylaxis [9]. Another study discovered that 4/12 (33%) patients with HB and 5/111 (5%) patients with severe HA experienced intracerebral bleeding during the 5 years, compared with no intracerebral bleeding in the HB patients [10]. Compared to Severe cases of HA and HB appear to have a milder bleeding type; however, intracranial bleeding appears to be more common in patients with severe HB. In light of the high in both types of coagulation disorders, bleeding can be life-threatening, it is essential for prophylaxis to be further studied for patients with severe or moderate HB.

Using three years of bleeding and factor concentration utilization data, Using bleeding frequencies and factor concentration utilization data, researcher conducted a study [11]. The difference in factor concentration usage per year between HA patients and controls wasn't statistically significant (14.4 bleedings per patient year compared to 8.63 bleedings per patient year), their results indicate that bleeding Patients with HA are more likely to suffer from this condition than those with HB. As well, another study found that age and hepatitis C and HIV infections did not confound the differences [12, 13]. Retrospective studies have numerous limitations, including incomplete patient histories and the lack of genotyping of HA and HB for molecular testing, as well as the inability to evaluate Prothrombin G20210 and FV G20210A are two modulators that may be used [14,15]. Any retrospective study is bound to have limitations, including the inability to obtain all of these data from patients.

**Conclusion**

According to our study, bleeding/(patient year) was statistically significant in HA patients compared to HB patients, indicating that HA patients are more likely to bleed. Consequently, our findings support previous observations Bleeding is less frequent among HB patients than among HA patients, corroborating previous observations that HB patients do not. Additionally, it is unclear if FVIII does not exist, compared to FIX, which leads to more bleeding. There is also no consensus on whether the bleeding has become more severe or whether the treatment is less effective. The clinical community should therefore plan fewer primary prophylactic treatments for patients with HB. Despite the low prevalence of hemophilia, progress toward larger samples within multiple centers is strongly recommended Since single-institution hemophilia rates are low studies.

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