

Hemophilic arthropathy: clinical, radiologic, and functional evaluation: a single-center experience in a limited resource country

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Introduction

Hemophilia A and B are clinically indistinguishable and are heterogeneous disorders. The severity of bleeding symptoms correlates with the coagulant activity of the deficient factor. Joint bleeding initially leads to independent adverse changes in both the synovial tissue and the articular cartilage.

Aim

The aim of the present work was to evaluate hemophilic joints clinically, radiologically, and functionally in patients with hemophilic arthropathy.

Materials and methods

The study was carried out on 30 boys suffering from hemophilic arthropathy; the mean age was 10.6 ± 2.95 years. All patients were subjected to thorough history taking and local physical examination of the 'target joint'. Functional Independence Score in Hemophilia (FISH) and the Pettersson scoring system were assessed for all patients.

Results

The age at first hemarthrosis decreased with the severity of hemophilia, whereas the number of bleeds/year and the number of joints affected increased with the severity, and the results were statistically significant. A statistically significant positive correlation was found between the Pettersson score and both the age of the patients and the number of bleeds/year. However, a negative correlation was found with factor activity level. In contrast, the FISH score had a significant positive correlation with factor activity level.

Conclusion

A significant decrease in the functional ability was demonstrated on the basis of the severity of hemophilia. Both the FISH and Pettersson scoring systems are of great importance in assessing patients with hemophilic arthropathy.

Keywords:

Functional Independence Score in Hemophilia, hemophilic arthropathy, Pettersson scoring system

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Introduction

Hemophilia A and B are clinically indistinguishable and are heterogeneous disorders [1,2]. Their clinical manifestations are identical, with an increased tendency for musculoskeletal, soft tissue, and mucocutaneous bleeding. The activity level of the deficient factor affects the severity of bleeding [1,3,4].

Spontaneous bleeding into a joint (hemarthrosis) and muscle is the most frequent manifestation of severe hemophilia. Joint bleeding accounts for 90% of bleeding in hemophilic patients [1,5]. Joint bleeding initially leads to independent adverse changes in both the synovial tissue and the articular cartilage. Both synovial inflammatory changes and cartilage damage affect each other [6].

Hemarthroses also have their impact on bone. Enlargement of the epiphysis and growth disturbance

are present in hemophilic patients as a sequelae of repeated joint bleeds; moreover, subchondral changes may occur in the form of osteoporosis, subchondral cyst formations, and both erosions and osteophyte formation. Furthermore, in severe forms of hemophilic arthropathy, ankylosis, fusion of the bones can occur; a phenomenon also observed in severe osteoarthritis [7,8].

The Pettersson score is a detailed radiologic classification of hemophilic joints that has been adopted by the World Federation of Hemophilia (WFH). It estimates joint destruction radiologically [9].

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Gilbert score is a physical examination score. It assesses joint health in patients with hemophilic arthropathy [10,11].

Functional Independence Score in Hemophilia (FISH) is a performance-based instrument used to objectively assess musculoskeletal function of patients with hemophilia. FISH measures the patient's independence in performing seven activities under three categories: self-care (grooming and eating, bathing, and dressing), transfers (chair and floor), and mobility (walking and step climbing) [12].

The aim of the present work was to evaluate hemophilic joints clinically, radiologically, and functionally.

Materials and methods

The study was carried out on 30 boys with hemophilia and with a history of previous joint bleeding. They were selected from those attending the Outpatient Hematology Clinic of Alexandria University Children's Hospital at Elshatby. All patients had at least one target joint. 'Target joint' was defined as a joint with a history of clinical symptoms of pain, tenderness, swelling, or locking.

This study was explained to the participants, and informed consent was taken from parents of all children included in the study.

All hemophilic patients included in the study were subjected to the following:

- (1) History taking, including age at first hemarthrosis (years), the number of bleedings (last year) and number of joints affected, and family history of similar condition.
- (2) Assessment of factor activity level: mild (5–40% of normal activity), moderate (1–5% of normal activity), and severe (<1% of normal activity) [3,4].
- (3) Evaluation of the target joint using the WFH clinical score (Gilbert score) [10,11].
- (4) FISH [12].
- (5) Conventional frontal and lateral radiographs of the target joint, which was scored according to the Pettersson score by a radiologist [9,11].

Statistical analysis of the data

Data were analyzed using Statistical Package for Social Sciences, version 20.0, 2nd ed. (2002; London, New York, Arnold). Qualitative data were described using number and percentage. Quantitative data were described using mean, SD median, and minimum and maximum. For abnormally distributed data

(data distribution that was significantly deviated from normal), more than two populations were analyzed using the Kruskal–Wallis test. Correlations between two quantitative variables were assessed using Spearman's coefficient.

Significance was considered at *P* value less than 0.05.

Results

The age of the studied boys ranged from 6 to 16 years, with a mean of 10.6 ± 2.95 years. Among the 30 hemophilic patients, 26 (86.7%) patients had hemophilia A and four (13.3%) patients had hemophilia B. Nineteen (63.3%) patients had a positive family history of similar condition and 50% of the patients had positive consanguinity.

The knee was the most affected joint in 22 (73.3%) patients, followed by ankle in five (16.7%) patients, only two (6.7%) patients had elbow affection, and one (3.3%) patient had shoulder affection.

Fifteen (50%) of the studied hemophilic patients had severe hemophilia, seven (23.3%) patients had moderate, and eight (26.7%) patients had mild hemophilia.

The age at first hemarthrosis decreased with the increased severity of hemophilia, whereas the number of bleeds/year and the number of joints affected increased with the increased severity and the results were statistically significant ($P = 0.001$, $P < 0.001$, and $P = 0.048$, respectively) (Table 1).

Clinical evaluation of the target joint using the Gilbert score is presented in Table 2. There was a significant inverse correlation between the WFH clinical (Gilbert) score and factor activity level ($r = -0.538$, $P = 0.002$) (Fig. 1).

FISH score was highest in patients with mild hemophilia, with a mean of 28.5 ± 2.38 , and the lowest among those with severe hemophilia, with a mean of 26.07 ± 4.27 , and this result showed statistical significance ($P = 0.036$) (Table 3).

There was a significant positive correlation between the FISH score and factor level ($r = 0.602$, $P < 0.001$) (Fig. 2).

There was a significant positive correlation between the Pettersson score and the age of the patients and number of bleeds/year (Fig. 3a and b).

Moreover, Pettersson score had a statistically significant negative correlation with factor activity level (Fig. 4).

Table 1 Relationship between factor activity level and bleeding history (age at first hemarthrosis, number of bleeds/year, and number of joints affected) in hemophilic patients

Bleeding history	Factor level			Total	Test of significance
	Mild (<i>n</i> = 8)	Moderate (<i>n</i> = 7)	Severe (<i>n</i> = 15)		
Age at first hemarthrosis (years)					
Minimum–maximum	2.0–5.0	3.0–5.0	0.5–4.0	0.5–5.0	^{KW} <i>P</i> = 0.001*
Mean ± SD	4.13 ± 1.13	4.43 ± 0.79	2.22 ± 1.16	3.24 ± 1.48	
Median	4.50	5.0	2.0	3.0	
Number of bleeds/year					
Minimum–maximum	3.0–5.0	4.0–5.0	4.0–8.0	3.0–8.0	^{KW} <i>P</i> < 0.001*
Mean ± SD	3.38 ± 0.74	4.71 ± 0.49	6.07 ± 0.96	5.03 ± 1.40	
Median	3.0	5.0	6.0	5.0	
Number of joints affected					
Minimum–maximum	4.0–6.0	1.0–8.0	4.0–12.0	1.0–12.0	^{KW} <i>P</i> = 0.048*
Mean ± SD	4.63 ± 0.74	4.57 ± 2.64	6.93 ± 2.43	5.77 ± 2.42	
Median	4.50	5.0	7.0	5.0	

KW, Kruskal–Wallis test; *Statistically significant at *P* ≤ 0.05.

Table 2 Clinical joint evaluation of the target joint among the hemophilic patients

Pain (<i>n</i> = 30) [<i>n</i> (%)]	Bleeding (<i>n</i> = 30) [<i>n</i> (%)]
No: 5 (16.7)	None: 8 (26.7)
Mild: 6 (20.0)	No major to 1–3 minor: 6 (20.0)
Moderate: 9 (30.0)	1–2 major or 4–6 minor: 7 (23.3)
Severe: 10 (33.3)	3 or more major or 7 or more minor: 9 (30.0)
Swelling (<i>n</i> = 30) [<i>n</i> (%)]	Muscle atrophy (<i>n</i> = 30) [<i>n</i> (%)]
No: 11 (36.7)	None or minimal < 1 cm: 18 (60.0)
Present: 9 (30.0)	Present: 12 (40.0)
Present+chronic synovitis: 10 (33.3)	
Axial deformity in the knee (<i>n</i> = 22) [<i>n</i> (%)]	Axial deformity in the ankle (<i>n</i> = 5) [<i>n</i> (%)]
Normal = 0–7° valgus: 5 (22.7)	No: 1 (20.0)
8–15° valgus or 0–5° varus: 8 (36.4)	Up to 10: 2 (40.0)
>15° valgus or >5° varus: 9 (40.9)	>10: 2 (40.0)
Crepitus on motion (<i>n</i> = 30) [<i>n</i> (%)]	Range of motion (<i>n</i> = 30) [<i>n</i> (%)]
None: 10 (33.3)	Loss of 10%: 9 (30.0)
Present: 20 (66.7)	Loss of 10–33%: 9 (30.0)
	Loss of >30%: 12 (40.0)
Flexion contracture (<i>n</i> = 29) [<i>n</i> (%)]	Instability (<i>n</i> = 30) [<i>n</i> (%)]
<15 FFC: 14 (49.0)	None: 5 (17.4)
>15 FFC: 15 (51.0)	Noted on examination without functional interference: 7 (23.3)
	Instability with function deficit: 18 (60.0)

FFC, fixed flexion contracture.

Table 3 Relationship between the Functional Independence Score in Hemophilia score and the factor activity level among hemophilic patients

FISH score	Factor level			<i>P</i>
	Mild (<i>n</i> = 8)	Moderate (<i>n</i> = 7)	Severe (<i>n</i> = 15)	
FISH score				
Minimum–maximum	27.0–30.0	25.0–32.0	18.0–36.0	0.036*
Mean ± SD	28.50 ± 0.93	28.0 ± 2.38	26.07 ± 4.27	
Median	28.50	28.0	26.0	

P, *P* value for Kruskal–Wallis test; *Statistically significant at *P* ≤ 0.05.

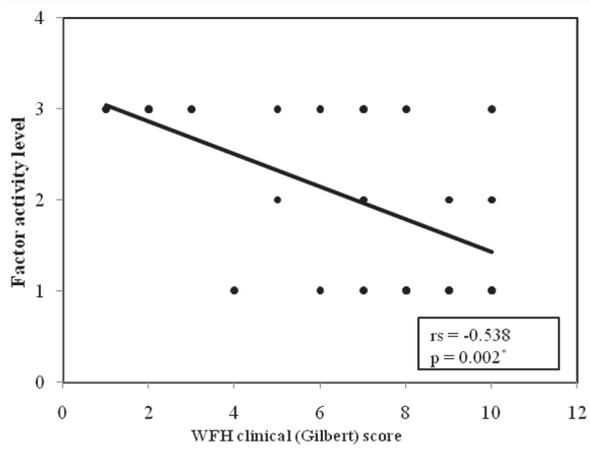
Discussion

Hemophilic arthropathy is the consequence of recurrent bleeding into the joint in patients with hemophilia and is the main cause of morbidity in these patients. This

study was carried out to evaluate hemophilic joints clinically, radiologically, and functionally.

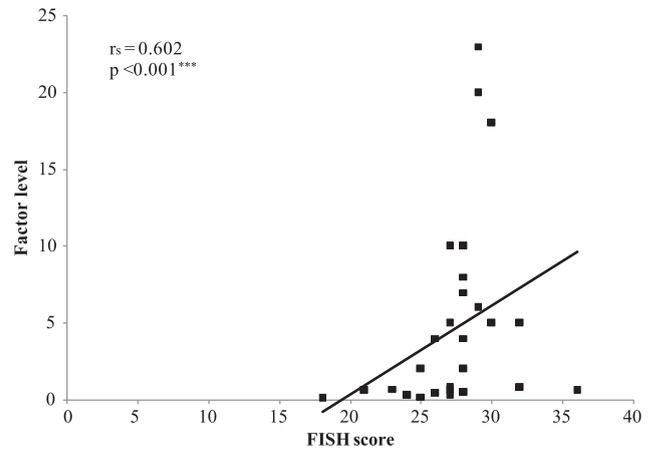
The most commonly affected joint in the present study was the knee in 73.3% of the cases, ankle in 16.7% of

Figure 1



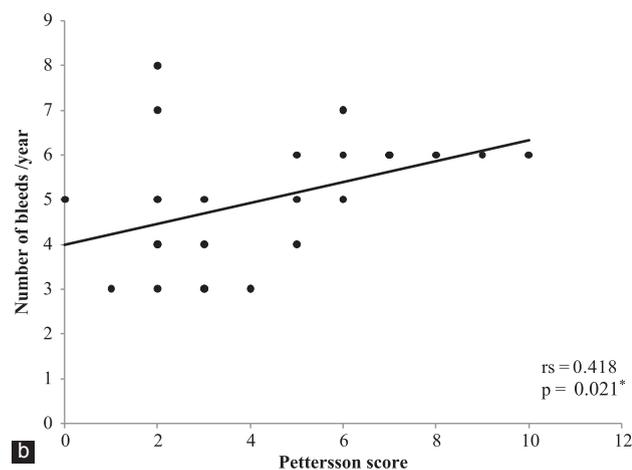
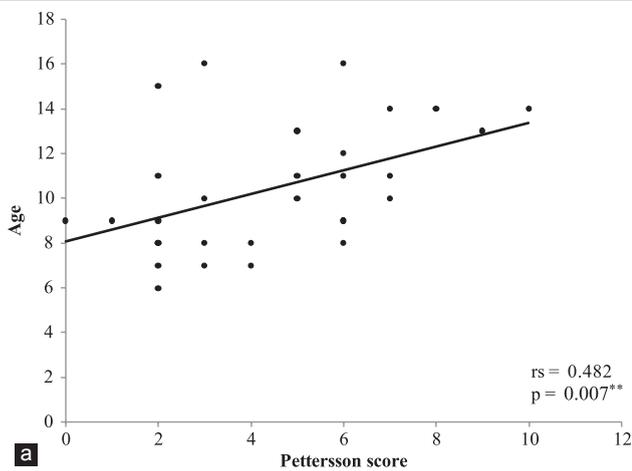
Correlation between World Federation of Hemophilia (WFH) clinical (Gilbert) score and factor activity level.

Figure 2



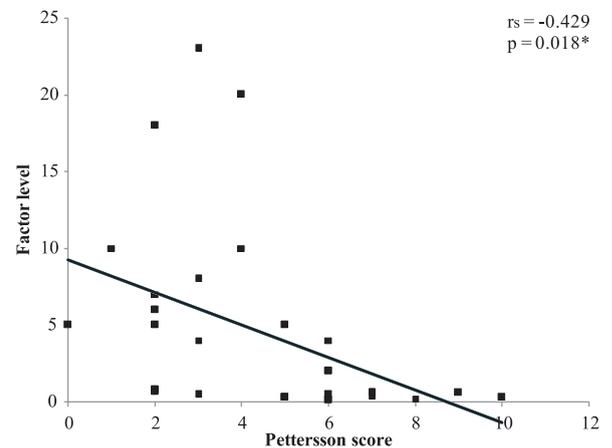
Correlation between Functional Independence Score in Hemophilia (FISH) score and the factor level.

Figure 3



(a, b) Correlation between Pettersson score and the age of patients and the number of bleeds/year.

Figure 4



Correlation between the Pettersson score and factor activity level.

cases, elbow in 6.7% of cases, followed by shoulder in 3.3% of cases (one patient). This finding is in agreement with that of Jansen *et al.* [13], who found that the three large joints (ankle, knee, and elbow) were the most

commonly affected. The knee and ankle have a weight-bearing function, as a result they bleed more often. Shoulders and hips are better supported and thus bleed less [14,15].

On comparing the bleeding history (age at first hemarthrosis, number of bleeds/year, and number of joints affected) with the severity of factor activity level, statistical significance was detected implying that a decrease in factor level resulted in lower age of hemarthrosis and increase in the number of bleeds/year, and an increase in the number of joints affected too. Data from the Universal Data Collection showed that patients with severe hemophilia were at a higher risk of developing a target joint than those with moderate or mild hemophilia (33.1 vs. 18.8% and 5%, respectively) [16].

Pollmann *et al.* [17] reported that, in nearly half of all children with severe hemophilia, the initial

hemarthrosis occurs during the first year of life. Fischer *et al.* [18] added that 90% of youngsters who are severely deficient in FVIII or FIX experience at least one joint hemorrhage before the age of 4.5 years.

In the present study, the mean age of first hemarthrosis in severe hemophilic patients was 2.22 ± 1 years and ranged from 0.5 to 4.0 years.

Individuals with severe hemophilia are more likely to develop joint problems and reduced range of motion (ROM) of joints [19,20]. ROM has been the most utilized measurement for evaluating the effects of intervention on joint health [21]. In the current study, 15 patients had severe hemophilia and seven patients had moderate, and all patients had limited ROM with variable degrees. ROM limitation increased significantly with more frequent bleeding episodes [20]. If patients with severe disease do not receive appropriate treatment, they will develop clinical symptoms: pain, swelling, and reduced ROM by early adolescence that will severely affect their health and quality of life [19,22,23].

In the current study, FISH score was significantly higher in those with mild hemophilia than in patients with moderate or severe hemophilia.

Because our patients receive on-demand therapy, the severity of the factor deficiency will increase the number of bleeds/year and thus more degenerative changes within the joint that correspondingly will impair patients' function. This was supported by previous studies [24,25].

The present study showed a statistically significant negative correlation between the Pettersson score and factor activity level. Similar results were reported by Hassan *et al.* [24]. Patients with severe degree of hemophilia have more radiological changes with Pettersson, as intra-articular bleeding accounted for more than 90% of all serious bleeding events in those patients [26].

Enlargement of epiphysis (30%) and irregular subchondral surface (32%) were the most frequent observation, whereas osteoporosis was less observed (13.3%). This was supported by Erlemann *et al.* [27], who studied the degree of osteoarthropathy in 40 hemophilic children using the Pettersson score.

Fischer *et al.* [18] reported that the Pettersson radiological score increases by 1 point for every three joint hemorrhages occurring after 5 years of age. In this study, the positive significant correlation between Pettersson score and number of joint bleeds/year was in accordance with that reported by Van Dijk *et al.* [28], who assessed joint damage using Pettersson

score based on age groups in severe hemophiliacs and reported that the score increased with the cumulative number of joint bleeds.

Conclusion

A significant decrease in the functional ability was demonstrated on the basis of the severity of hemophilia. The most commonly affected joints in patients receiving on-demand therapy are the knees, followed by the elbows and ankles.

In hemophilic patients, radiographic scoring of the joints using the Pettersson scoring system proved to be useful, available, and cheap for prediction of the degree of hemophilic arthropathy.

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The manuscript has been read and approved by all authors, that the requirements for authorship as stated earlier in this document have been met, and that each author believes that the manuscript represents an honest work.

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Conflicts of interest

There are no conflicts of interest.

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