

## Evaluation of Hemophilic Arthropathy in Children in Algiers Center

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### Abstract

Hemophilia is a hematological disease responsible for hemarthrosis starting from the age of learning to walk. In severe forms, these hemarthrosis are at the origin of hemophilic arthropathy that can lead to a loss of autonomy. The clinical and radiological evaluation of this arthropathy must be supplemented by a functional evaluation which will determine the impact of the disorders on the performance of activities of daily living and guide the therapeutic decision. The aim of the present work was to evaluate hemophilic joints clinically, radiologically, and functionally in patients with hemophilic arthropathy.

Our study concerned 43 patients with mean age of 9.17 +/-6.26 a total of 67 affected joints were assessed clinically by the Pednet score, radiologically by the Pettersson score and the functional FISH score. The knees are the most common joints followed by the elbows and ankles. There was a highly significant correlation between Pednet clinical score and Pettersson radiological score ( $P < 0.00001$ ,  $r = 0.769$ ) and between Pednet clinical score and FISH functional score ( $r = 0.03$  and  $P = 0.023$ ). Given the significant correlation between these scores, these scores can be extremely useful in clinical practice to detect early joint damage and guide therapeutic management.

**Keywords:** Hemophilia; Hemophilic Arthropathy; Orthopedic Score; Radiological Score; FISH Score

### Introduction


Hemophilia is a hematological disease characterized by a partial or complete deficiency of clotting factors VIII or XI [1]. Hemorrhagic manifestations predominate in the locomotor system, including hemarthrosis starting at the age of learning to walk.

In severe forms, these hemarthrosis are at the origin of deficiencies, such as the loss of muscle strength and joint stiffness responsible for irreversible joint damage that inevitably leads to disability [2].

Currently orthopedic sequelae in hemophilia are much less frequent and less severe due to the systematic prophylactic treatment

adopted by developed countries and by a good organization of care and management [3]. However, recent follow-up data at more than 20 years of severe hemophilia patients undergoing prophylaxis show that, even in the absence of clinical hemarthrosis, a certain number of these patients develop arthropathy mainly in the ankles [4].

The evaluation of joint involvement should be carried out in any hemophilia patient to establish a state of joint and muscle function and to allow its follow-up. It is recommended that the joints of a hemophiliac be evaluated every 6 months in children and every year in adults [5].



**Figure 1:** Hemophilic arthropathy of the knee.

Joint damage is universally assessed by orthopedic scores validated by the WFH, Gilbert's score for adults, it is an additive score with different items corresponding to:

- Pain,
- The frequency, the importance of episodes of hemarthrosis,
- Joint swelling,
- Limitation of the range of motion,
- Joint stability,
- Deformation in the frontal plane, presence of flexum,
- The presence of cracking at mobilization and amyotrophy.

This score of 0 to 3 for pain, from 0 to 3 for the assessment of episodes of hemarthrosis and from 0 to 12 for joint examination, is applied to each joint and an overall score can be calculated considering the most frequently affected joints namely the knees, elbows and ankles.

Paediatric orthopaedic scores have been developed by the Paediatric Committee of the World Hemophilia Federation and the European Paediatric Network for hemophilia management PEDNET.

Recently, the International Prophylaxis Study Group developed and validated a new, more sensitive pediatric clinical score, the hemophilia joint health score (HJHS) [6]. This score is also recommended to assess hemophilia patients who have arthropathies at the onset stage. This score has 10 items:

- Joint swelling,
- Duration of swelling,
- Muscle atrophy,
- Axial alignment,
- Crepitation during movements,
- Loss of flexion,
- Loss of extension,
- Instability,
- Joint pain,
- Muscle strength and gait disorders.

Each element is noted for each of the six joints (elbows, knees, and ankles), the maximum score for the six joints is 144.

### Radiological assessment

Standard X-rays (RX). Conventional radiography is the basic examination accessible to all, inexpensive. On the other hand, its use should be limited for a patient because of the deleterious effects of RX in case of prolonged or frequent exposures [7].

The radiological aspect of hemophilic joints is strongly correlated with the number of episodes of hemarthrosis. We can objectify:

- A dense joint effusion and sometimes, in young children, an enlargement of the joint space that can disappear in a few weeks during the initial episodes. With the multiplication of hemarthrosis the swelling of the periarticular soft tissues becomes permanent and can present in the periphery a dense border of hemosiderin; Peri-articular bone rarefaction.
- Epiphyseal hypertrophy in children, reactive to hyperemia. It will gradually contrast with the small character of diaphysis whose cortical is fine; Then very limited erosions typically starting at the areas of reflection of the synovial;
- A central irregular bone lamina and geodes under chondrals, often contrasting with the relative preservation of joint space;

- Then a typically diffuse joint pinching, sometimes with gearing of the articular surfaces, fragmentation of the banks and joint destruction; Finally, metaphyseal growth arrest streaks are reported.

Recently, in 1980 Pettersson [7] proposed a classification that makes it possible to establish a radiological score for each affected joint. It is an additive and analytical score that is recognized by the World Federation Of Hemophilia. This score results from the sum of the ratings (0 to 1: or 0 to 2) attributed to elementary radiological lesions:

- Osteoporosis
- Epiphyseal enlargement,
- Irregularity of the articular surface,
- Formation of cysts under chondralus,
- Pinching the line spacing,
- Erosion of the articular banks,
- Incongruence of articular surfaces and joint dislocation,

A Score zero corresponds to a radiologically normal joint, a score of 13 corresponds to the most impaired chronic arthropathy

**Figure 2:** Arthropathy of the knee: Epiphyseal hypertrophies contrasting with the hail character of the diaphysis, irregularity of the subchondral surface.

**Figure 3:** Knee arthropathy: geodic subchondral erosions, associated with joint pinching, marginal osteophytosis, with deformation of the articular surfaces and zero-rating.

### The ultrasound

The ultrasound is a non invasive, inexpensive repeatable examination without risk to the patient. It shows at the onset, a variable echostructural effusion, hyper vascular thickening of the synovium and blurring of the cartilage.

It makes it possible to differentiate between an intra-articular effusion and a synovial hypertrophy, it is very useful to follow the day-to-day evolution of an acute hemarthrosis. In advanced forms, thinning or irregularities of cartilage, subchondral erosions and fibrous synovial hypertrophy can be observed [8].

In hemophiliacs this examination is of major interest to highlight joint damage earlier than does the standard X-ray, but this examination has however a limited, it is operator dependent.

### Computed tomography

Computed tomography (CT) essentially analyzes bone tissue appreciating in particular the existence of erosions of joint surfaces, intraosseous geodes, rarefaction of the bone frame and hypertrophic deformities [7].

### Magnetic resonance imaging

It is much more accurate than all other imaging techniques, it shows joint alterations early. It can be used from the first episodes

of hemarthrosis while radiographies are still normal. It makes it possible to provide details on the state of the synovial, bone deficiencies, cysts under chondral, cartilage lesions and bone erosions as well as joint effusions.

Its limited accessibility, cost, and the need to perform it under sedation in young children are major drawbacks despite its excellent sensitivity [8].

**Figure 4:** Osteoarthropathy of the knee: hemarthrosis of medium abundance with hypertrophy of the synovial, osteochondral lesion of the internal femoral condyle and a geode of the internal tibial epiphysis, it is associated with a lesion of the post horn of the internal meniscus.

### Functional evaluation

Due to repeated hemarthrosis leading to a functional disability that can lead to a loss of autonomy, the clinical and radiological evaluation must be supplemented by a functional evaluation that will determine the impact of the disorders on the performance of activities of daily living, and guide the therapeutic decision.

Functional dependence Score Of Hemophilia (FISH) [10], The Hemophilia Functional Independence Score (FISH) was designed as a tool to objectively assess the musculoskeletal function of patients with hemophilia, and measure the patient's functional capacity [10]. FISH is relatively easy to perform. It is intended to complement other scores, such as clinical and radiological assessment scores. Its main advantage is that it can be used with people of different language abilities.

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

### Materials and Methods

The study was conducted on 43 boys with hemophilia and with a history of joint bleeding at the service of physical medicine and rehabilitation at the hospital Mustapha Algiers Algeria.

All hemophilic patients included in the study were subjected to the following : History taking, including age at first hemarthrosis, the number of bleedings (last year) and number of joints affected, and type and regimen of replacement therapy.

All patients were assessed by the Pediatric Orthopedic Clinical Score «Pednet», the Pettersson Radiological Score and the FSH Score.

### Statistical analysis of the data

Data were analyzed using Statistical is done on IBM SPSS 22 software and R version 3.2.5 software.

### Calculate the following statistical parameters:

Descriptive statistics

Percentage, mean, series mean matched, median, and standard deviation.

Analytical statistics

Qualitative variables: comparison of percentages by the khi two test and the Fisher test.

Quantitative variables

- Comparison of the means on series matched by the Student test «t» of the matched series with calculation of the significance threshold «P» and the confidence interval of the mean difference.
- Analysis of variance by the ANOVA test
- Use of linear regression and calculation of the correlation coefficient.
- Analysis of collinearity.

## Results

The mean age of children included was 9.17 +/-6.26 (range 4-16). All children had history of hemarthrosis.

(90,7%) of the studied hemophilic patients had severe hemophilia, (7%) patients had moderate, and (2.3%) patients had mild hemophilia.

The age at first hemarthrosis was 31.95 months.

55,8% of the children in study were on prophylactic therapy and 44,2% is on demand factor therapy.

The number of children having single affected joints were 56%) and multiple affected joints were 44%).

The knee was the most affected joint in (60%) patients, followed by elbow in (25%) patients, (15%) patients had ankle affection, The knees are the most affected joints with a score of 8,51 on left and 5,32 on right (Table 1).

Clinical evaluation of the target joint using the Pednet score, the mean score was 21,6 (Table 2).

The patient on prophylaxis and for patient treated on demand had respectively 17,7 and 27,47 (Table 3).

The mean radiologique score was 2,85, knees had highly score 3,7 (Table 4).

The mean FISH score was  $24.29 \pm 3.38$  (range 17-29) The activities that obtained the lowest score were squatting, running, step climbing and walking (Table 5).

There was a highly significant correlation between Pednet clinical score and Pettersson radiological score ( $P < 0.00001$ ,  $r = 0.769$ ).

and between Pednet clinical score and FISH functional score ( $r = 0.03$  and  $P = 0.023$ ) is presented in figure 1 and 2.

	Moy	SD	Min-Max
Score Total	21,6	14,17	06-72

**Table 2:** Mean clinical score per joint affected. Total score orthopédique (Pednet).

	Treatment on demand	Prophylaxique treatment	P
Score	27,47	17,17	0,019

**Table 3:** Total score total.

Joints	Number	Percentage (%)	Total Score	Average score per joint
Knees	40	59,7	148	3,7
Eblows	17	25,4	24	1,41
Ankles	10	14,9	19	1,9
Total	67	100	191	2,85

**Table 4:** The average radiological score per joint reached.

	Moy	Sd	Min-Max
Right knee	5,32	7,82	0-21
Left knee	8,51	8,32	0-21
Right ankle	1,39	3,79	0-14
Left ankle	0,76	0,767	0-15
Right elbow	2,69	6,03	0-22
Left elbow	2,9	5,82	0-18

**Table 1:** Orthopaedic clinical score for each joint.

The function	Eating	Washing	Getting dressed	Getting up	Climbing stairs	Walking	Squarring	Running
The score	3,68	3,61	3,58	3,07	2,95	3	2,65	2,26

**Table 5:** Functional Evaluation.

### Representation of the correlation between the clinical score (Pednet), and the different functional (FISH) and radiological scores

#### Pednet score depending OC FISH score

**Figure a:** Correlation between clinical score and functional score. Very significant correlation between Pednet clinical score and FISH functional score ( $r = 0.03$  and  $P = 0.023$ ).

#### Pednet score based on pettersson score

**Figure b:** Correlation between clinical score and radiological score. Very significant correlation between Pednet clinical and Pettersson radiological score ( $P < 0.00001$ ,  $r = 0.769$ ).

### Discussion

Hemophilia is a hematological disease whose functional prognosis is related to orthopedic manifestations. The latter are the cause of morbidity and source of disability in these patients.

The study involved 43 hemophilia patients; the mean age of the study population is  $9.17 \pm 6.26$  years. This is a young population, because in hemophiliacs it is recommended to prevent hemophilic arthropathy especially in the growth phase of the child.

The initial hemarthrosis occurred in 58% of our patients at an average age of 31 months. Our result is consistent with the study by Pollmann, *et al.* [11], which reported that in nearly half of children with severe hemophilia, the initial hemarthrosis occurs during the first year of life. Another recent study done in 2016 by Abdelghani H., *et al.* [12] found an average age at the first hemarthrosis of  $2.2 \pm 1$  year. The site of the first hemarthrosis in our patients was the knee in more than half of the cases. This is explained by the fact that the first hemarthrosis occurs from the first steps. From the acquisition of walking, the knees are the most exposed joints.

More than half of our patients (56%) were on prophylactic treatment, thanks to the many actions that have been taken to improve the management of hemophiliacs in Algeria [10].

90% of our patients had one to two joints affected, three patients had 3 joints affected and only one patient had 4 joints affected. As a result, we treated 67 joints, including 40 knee joints, 17 elbow joints and 10 ankle joints. The most affected joints are the knees, elbows and ankles and this is in line with the study by Jansen, *et al.* [13], which found that the 3 large joints (knees, elbows and ankles) are the most frequently affected because they are synovial type joints. They bleed more often but the hips and shoulders rarely bleed. The average clinical score per patient according to the treatment received found a better clinical score of patients on prophylactic treatment compared to those treated on demand with a significant difference between the two treatments ( $p < 0.02$ ).

These results are in line with those of several authors who confirm the superiority of prophylactic treatment over on-demand treatment in order to prevent hemorrhages, in particular osteoarticular localizations [14].

A radiological assessment by a Pettersson score was performed in our 43 patients. An average radiological score per joint was calculated for each patient. The knee is the most radiologically affected joint with an average score per joint at 3.7, followed by the ankles with a score of 1.9 and then the elbows with a score of 1.4. Our results are similar to those of Hassan, *et al.* [15], who found that the knee is the most radiologically damaged joint with a score of 2.32, followed by ankles at 1.86 and finally elbows with an average score at 1.42. Another study done by Van Dijk, *et al.* [16] who evaluated joint damage using the Pettersson score in severe hemophiliacs,

reported that the score increases with the cumulative number of joint bleeding.

All patients over 5 years of age were assessed by the FISH score. The most affected activities were running, squatting and climbing stairs, these results could be explained by the fact that in our study knee involvement was the most common. These results are consistent with the results of the majority of other studies published in the literature. A Mexican study by Tlacuilo-parra A., *et al.* [17], evaluated 90 middle-aged hemophiliac children of 10.0+/-3.4, each patient was evaluated in seven activities (running was not evaluated so the score was between 7 and 28), the average score was 25.8+/-3.6 and the most affected activities were walking, squatting and climbing stairs. Another study done by Hassan T H., *et al.* [15], performed a functional assessment by the FISH score in 50 adolescents, the average score out of 28 was 23.32+/-4.69 and the most affected activities were walking, squatting and climbing stairs.

In addition, there was a significant correlation between the Pettersson score and the clinical score ( $P < 0.00001$ ,  $r = 0.769$ ), as well as a correlation between the FISH functional score and the Pednet orthopaedic clinical score ( $r = 0.30$  and  $P = 0.023$ ).

## Conclusion

Hemophilic arthropathy, the main complication of hemophilia, leads to impaired quality of life in hemophilia patients. Pednet clinical scores and Pettersson's radiological score can be extremely useful in clinical practice and considered very sensitive in detecting early joint damage to guide therapeutic decision and the FISH score appears to be a reliable tool for assessing the functional independence of these patients.

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## Conflict of Interest

None.

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