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Radiological and clinical evaluation of hemophilic arthropathy in Egyptian patients

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Abstract

Background: In hemophilic patients, recurrent hemorrhages in the same joint lead to significant hypertrophic synovitis followed by progressive cartilage degradation. Gross arthritic alterations have been evaluated by clinical scoring and plain radiography scores. At present, magnetic resonance imaging (MRI) seems to be the most accurate radiological technique in joint assessment of the articular and periarticular structures.

Aim: To assess arthritic changes clinically and radiologically by plain radiography and MRI and correlate the 3 scoring systems as well as to correlate these findings with the number of joint bleeds.

Patients and methods: The study was conducted on 20 patients with Hemophilia A and B and one patient with type 3 von Willebrand disease. Twenty-six joints were assessed clinically by the orthopedic score and the radiologically by Arnold Hilgartner score and 17 were assessed by MRI as well using the Denver and the European scores.

Results: On the radiological evaluation, the main changes were an enlarged epiphysis and osteoporosis whereas the MRI findings included cysts, erosions, synovial hypertrophy, hemosiderin deposits and effusion. Correlation of the clinical score with the x-ray was non significant but that with the Denver MRI score was significant (r= 0.6, p= 0.02) as well as that of the plain x-ray and Denver score (r= 0.6, p= 0.007).The number of joint bleeds per year correlated significantly with plain x-ray and MRI scores (r= 0.5, p= 0.01*; r= 0.5, p= 0.02 and r= 0.6, p= 0.02*) respectively but not with the clinical score.

Conclusion: The available clinical and radiological scoring detects the more advanced changes in hemophilic children. However, MRI is a sensitive diagnostic tool in documenting early changes especially in those with no obvious clinical signs; therefore it plays a role for the selection of patients on demand or prophylactic treatment.

Keywords

Hemophilic arthropathy, clinical scale, MRI scoring system, Arnold Hilgartner score

Introduction

Hemophilia is an X-linked recessive disease due to reduced plasma levels or absence of factor VIII (FVIII: C) or factor IX (FIX: C) which predispose to hemorrhages where 92% of all bleeding episodes occur in joints. Hemophilic arthropathy due to recurrent hemarthrosis is the main clinical feature of severe hemophilia and a major cause of morbidity in this group especially for those not on a prophylactic scheme.[1] Hemarthrosis occurs most commonly in the knees, elbows and ankles[2,3] but can also occur in other joints. Recurrent hemorrhages in the same joint lead to significant hypertrophic synovitis followed by progressive cartilage degradation eventually resulting in hemophilic arthropathy expressed clinically with significant functional impairment of the joint.[4] Synovitis causes hypertrophy of the epiphysis that may lead to leg length discrepancies and angular deformities in children.[5]

For decades, gross arthritic alterations have been evaluated by clinical scoring[6] and plain radiography using two main classification systems; the Arnold-Hilgartner and the Pettersson scales,[7,8] respectively. However, plain radiography does not detect early changes in soft tissues as the synovium and the cartilage. At present, magnetic resonance imaging (MRI) seems to be the most accurate radiological technique in joint assessment. It allows precise non- invasive study of all the articular, synovium, cartilage, bone and periarticular structures. It reveals hypertrophic synovial tissue, articular cartilage damage, as well as more advanced alterations of hemophilic arthropathy when compared with those documented by plain X-ray.[4] It is particularly sensitive for early preclinical stages of hemophilic arthropathy still undetectable by conventional radiography.[9]

Several MRI based methods for scoring joints have been presented,[10-17] but still the experience of correlating such scores with clinical data is very limited.[12,14] It is important to analyze MRI changes in hemophilic arthropathy and their relation, to clinical parameters to enable selection and refinement of useful scoring methods.[19] Two of the most widely used scoring systems are the Denver[11] which is based on a progressive method rated by the most severe change and the European scale[16] based on an additive method that displays osteochondral and soft tissue related changes.

The aim of our study is to assess arthritic changes clinically and radiologically by plain radiography and MRI in patients with hemophilia and Von Willebrand disease and correlate the

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3 scoring systems with each other as well as with the number of joint bleeds.

Patients and methods

Study group

The study was conducted on 20 patients who were followed up at the Hemophilia outpatient clinic, located at Cairo University Pediatric Hospital their ages ranged from 2 to 21 years with a interquartile mean of 12 (7.1-16.0).

Five boys had severe hemophilia A (FVIIIC <1%), 10 moderate hemophilia A (FVIII: C= 1-5%) and one mild (FVIII: C= 8.4%). Two patients had moderate hemophilia B. The study also included 2 girls, one with moderate hemophilia A, who has a hemophilic father and another with von Willebrand disease type 3. Only one patient with a low titre of factor inhibitor. Six of them were positive for hepatitis C by ELISA but all were HIV negative by PCR.

Twenty-six joints were evaluated beyond acute bleeding episodes, clinically by thorough examination of the joint affected by an expert physician. The physical examination score of the Orthopedic Committee of the World Federation of Hemophilia[6] was used for this purpose; this score has a maximum of 12 points for each joint. Twenty-one were target joints with more than three bleeds in the same joint.

Radiologically, all 26 joints were assessed by plain X-ray (17 knee, 2 elbow, 2 hip, 5 ankle) but only 17 joints (11 knee, 2 ankle, 2 elbow and 2 hip) were evaluated by MRI as well. Those represented patients aged ≥8 years. We further assessed seventeen asymptomatic joints with no history of bleeds both clinically and by X-ray.

All our Hemophilia A patients and the one with von Willebrand disease type 3 are on demand therapy receiving double virally inactivated plasma derived factor concentrate and/or cryoprecipitate according to resource availability. Those with hemophilia B receive fresh frozen plasma. None of our patients are on prophylaxis due to resource constraint, an informed consent was obtained.

Imaging methods

Plain radiography

All patients were subjected to conventional X-ray studies in at least two basic projections (AP or PA and lateral or oblique) on the affected joint and in some cases X-rays of the corresponding normal joint were also done for comparison. X-rays findings were assessed using Arnold-Hilgartner scoring system ranging from 0 to 5[7] where the final score is given to the worse findings in the joint as one advances through the different stages of the disease. Joint changes include in order of severity; soft tissue swelling, osteoporosis, overgrowth of epiphysis, subchondral bones cysts, squaring of the patella, joint space narrowing and loss of cartilage. Stage 5 includes the worst changes in the form of fibrous joint contracture, extensive enlargement of the epiphysis and substantial disorganization of the joint.

MRI parameters

MRI studies were performed using a (Philips Gyroscan Intera (1.5 T) super conducting magnet). The MRI protocol included the following sequences to cover the expected findings of hemophilic arthropathy. The sagittal T1 weighted sequence (TR 418 ms, TE 12 ms, slice thickness 3 mm field of view 100mm, matrix 184 x 256, two acquisitions), a sagittal T2 weighted Turbo Spin Echo sequences (TR 4200 ms, TE 96 ms, slice thickness 3 mm, FOV 10 mm, matrix 154 x 256, two acquisitions), a sagittal fat-suppressed 3 D gradient echo sequence (TR 50ms, TE 11 ms, flip angle 40°, slice thickness 1.5 mm, matrix 228 x 256, one acquisition) and a coronal short tau inversion recovery (STIR) sequence T1 (TR 4500 ms, TE 60 mms, slice thickness 4 mm, FOV 113 mm, matrix 198 x 256, three acquisitions). MRI findings were assessed using Denver and European scoring systems which comprise two compatible scales for progressive and additive assessment of hemophilic arthropathy.[11,16] The Denver score ranges from 0 to 10 and it evaluates the different stages of pathological development in relation to the most severe finding. It includes assessment of presence of effusion, hemarthrosis, synovial hyperplasia, hemosiderin deposits, erosion, subchondral cysts, cartilage loss as well as the presence of some ancillary findings as pseudotumour. It considers the highest grade given to a joint as the final score and so the maximum final score is 10.The additive European MRI score is given in the format A (e:s:h)* and with a maximum score of 16 (4:4:4). The scoring system grades the effusion/hemarthrosis(e), synovial hypertrophy(s)/hemosiderin(h) components with values ranging from 0 to 4 and the A-components with values that correspond to the sum of the sub items assigned for the items of the A-category.

Statistical analysis

Statistical Package for social science (SPSS) version 9.0 was used for data analysis. The data was summarized as percentage, median, interquartile range and Chi Square test which was used for analysis of qualitative data. Spearman rho correlation coefficients were also calculated. The correlation coefficient(r) was considered as very weak if <0.25, mild ≥0.25-<0.5, moderate if ≥0.5-<0.75 and strong if ≥0.75. P-value is considered significant if ≤0.05.*

Results

The study included 20 patients, 18 males (90%) and 2 females (10%). Those included 17 patients with Hemophilia A, 16 males and one female the daughter of a hemophiliac father. Five were severe (29.4%), 11 moderate (64.7%) and one mild (5.9%). The remaining patients included 2 with moderate hemophilia B and one with von Willebrand disease type 3. We assessed 26 symptomatic joints clinically and by plain X-ray; 17 (65.4%)

TABLE 1

Orthopedic score and Arnold Hilgartner score of 26 symptomatic joints

No	*Age (yrs)*	*Diag.*	*Joint involved*	*No. of bleeds/yr*	**Clinical score*	***Plain X-ray score*
1	4 yrs	Hem A	LA	3	1	0
2	12	Hem A	LK	4	4	4
3	12	Hem A	RK, LK, LE	12, 8, 3	10, 10, 12	4, 2, 0
4	10	Hem A	RK	6	11	5
5	3.0	Hem A	RK, LK	4, 4	2, 2	2, 2
6	2.0	Hem A	RK	4	2	2
7	16.0	Hem A	RH	4	0	4
8	17.0	Hem A	RK	4	4	4
9	21.0	Hem A	RH	5	7	5
10	11.0	Hem B	LK	5	3	5
11	9.0	Hem A	RK	2	1	2
12	18.0	Hem A	E, K, A	6, 10, 4	5, 5, 4	0, 4, 0
13	9.0	Type 3 VWD	RA	5	10 + S	0
14	14.0	Hem A	LK	3	3	0
15	3.0	Hem A	RK	4	0	2
16	12.0	Hem A	LK, RA	10,10	5, 6 + S	4, 5
17	14.0	Hem A	LK	4	6	2
18	16.0	Hem A	RK	1	8	3
19	8.0	Hem A	RA	3	8	0
20	4.0	Hem B	RA	6	2	2

HemA: hemophilia A; HemB: hemophilia B; LA: left ankle; LE: left elbow; LK: left knee; RA: right ankle; RH: right hip; RK: right knee; S: swelling; VWD: Von Willebrand disease; Yrs: years.
*Clinical score: Physical examination score according to World Federation of Hemophilia.[6]
**X-ray score: Arnold Hilgartner score.[7]

TABLE 2

Arnold Hilgartner[7] and MRI***[11,16] score of 17 joints**

Pt	*Joint involved*	*Plain X-ray score** (Arnold Hilgartner)*	*MRI score*** (Denver and European)*
1	LK	4	6
2	RK, LK, LE	4, 2, 0	9, 10, 3
3	RK	5	11
4	RH	4	4
5	RH	5	5
6	LK	5	4
7	RK	2	3
8	E, K, A	0, 4, 0	6, 5, 2
9	RA	0	3
10	LK	0	1
11	LK	2	4
12	RK	3	8
13	RA	0	1

LA: left ankle; LE: left elbow; LK: left knee; RA: right ankle; RH: right hip; RK: right knee;

knee, 2 (7.7%) elbow, 2 (7.7%) hip and 5 (19.2%) ankle. The right side is usually more affected than the left. Only 17 joints; 11 (64.7%) knee, 2 (11.8%) ankle, 2 (11.8%) elbow and 2 (11.8%) hip were evaluated by MRI as well.

On clinical evaluation using the physical examination score of the Orthopedic Committee of the WFH, the score ranged from 1 to 12 with a median of 4.5 (interquartile range, 2.0-8.0) (table 1). The abnormalities ranged from crepitus on motion and mild muscle atrophy to impaired range of motion, axial deformity and swelling due to chronic synovitis. Patients with mild clinical involvement having scores of 1 to 3 had X-ray scores ranging from 0 to 5 and the three evaluated by MRI had a score of 1 to 4. No abnormalities were detected on clinical evaluation of only 2 joints (7.7%). One patient is a 3-year old

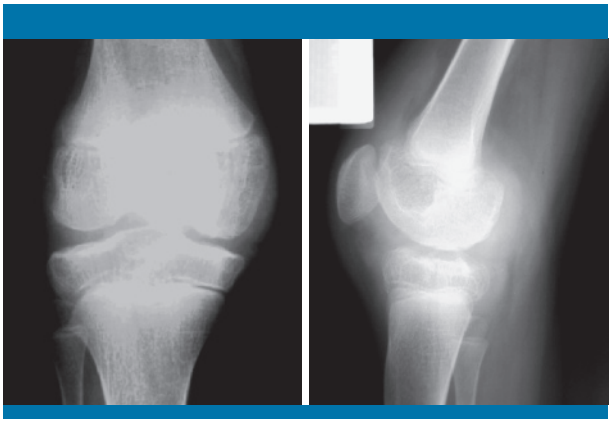

Figure 1. (a) *Comparative images with conventional radiography and MRI of the left knee of a 10 year girl with hemophilia A Plain X-ray showing enlarged epiphysis, widened femoral notch and square patella with narrow joint space*

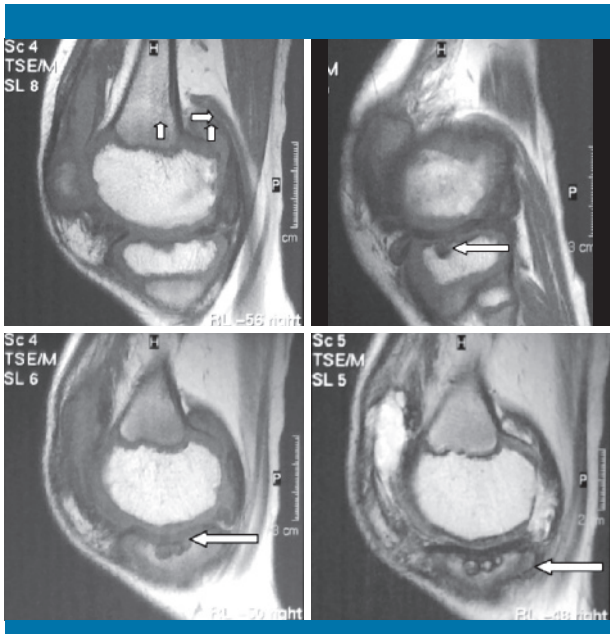

Figure 1. (b) *MRI of the knee in sagittal T1 and T2 weighted images showing surface erosion with cortical irregularities of the distal femur and proximal tibial (better seen on T 1 weighted image, small arrows). Multiple subchondral cysts in the proximal tibial epiphysis (intermediate on T1-weighted image and shows small bright focus on T2- weighted image, large arrows), and a focal defect of the overlying cartilage is revealed*

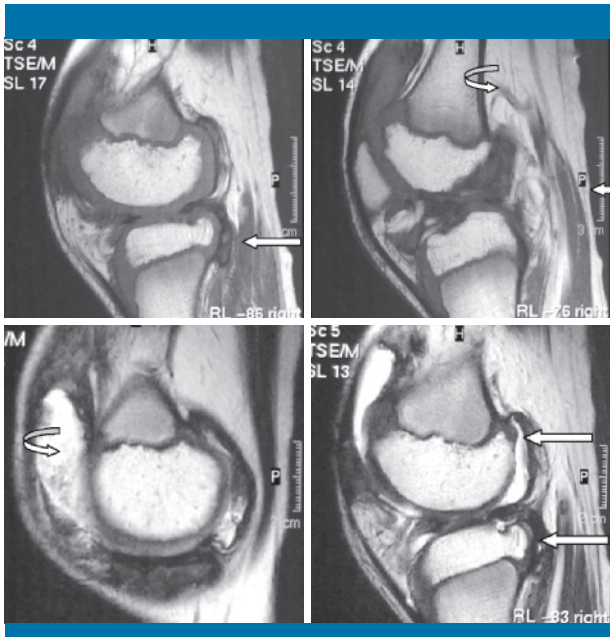

Figure 1. (c) *MRI in sagittal T1 and T2 weighted images which shows a hypertrophied synovium with hemosiderin deposition seen on both T1 and T2 weighted images (large arrows) and joint effusion is also noticed (curved arrow)*

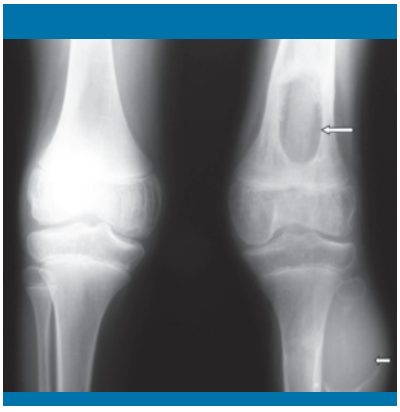

Figure 2. (a) *X-ray AP of a 12 year old with moderate hemophilia A showing a hemophiliac pseudotumour. There is a large osteolytic lesion of the femur (large arrow) and a huge expansile destructive lesion of the fibula (small arrow) as well as changes of hemophilic arthropathy*

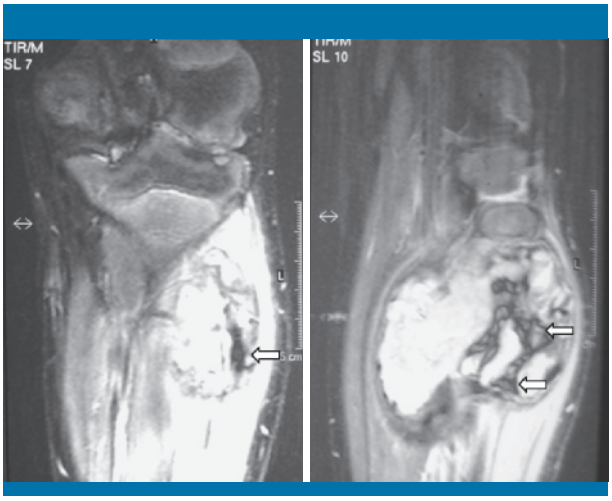

Figure 2. (b) *MRI Coronal T1 STIR of the same patient's left knee showing the pseudotumour of the proximal shaft of the fibula with dark signal intensity areas of chronic blood products (arrow)*

with severe hemophilia and a history of 4 bleeds with a score of 2 on plain radiography while the other is a teenager with moderate hemophilia A. He had scores of 4 and 4 on X-ray and MRI scales respectively though he had a history of less than 3 bleeds of his hip joint.

On plain radiological assessment by Arnold Hilgartner scale, 18 joints had a score ranging from 2.0 to 5.0 with a median of 2.0 (interquartile, 0.0-4.0) (table 1).The main radiological alterations were enlarged epiphysis and osteoporosis. Six joints showed narrowing of joint space and squaring of the patella (figure 1a). One of our patients had a pseudotumour discovered accidentally which was resolved partially on replacement therapy (figure 2).

Seven joints (44.4%) showed no abnormality though they showed some clinical signs. We further assessed six of these joints by MRI and all showed some changes with scores ranging from 1 to 6. Those with scores ≥3 by Arnold Hilgartner had MRI scoring ranging from 4-11 with synovial hypertrophy in

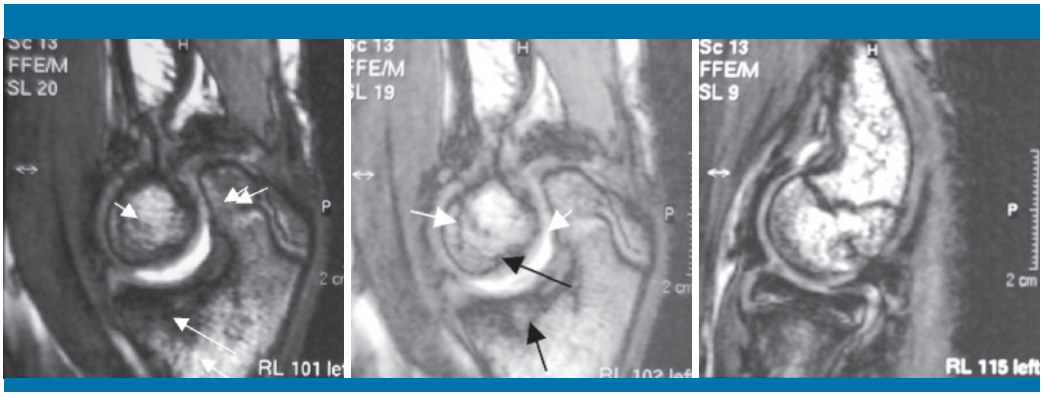

Figure 3. *An 18 year old patient with moderate hemophilia A. A MRI of the left elbow sagittal T2 FFE shows surface cortical erosions with dark signal intensity on the humeral and ulnar surfaces (long arrows), mild synovial hypertrophy with confluent hemosiderin deposition (short arrows)*

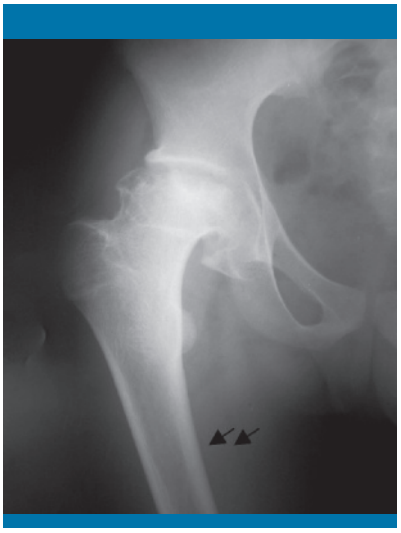

Figure 4. (a) *21 year old patient with moderate hemophilia A. X -ray of the right hip AP view showing secondary hemophilic osteoarthritis with femoral cortical irregularities and subchondral cysts*

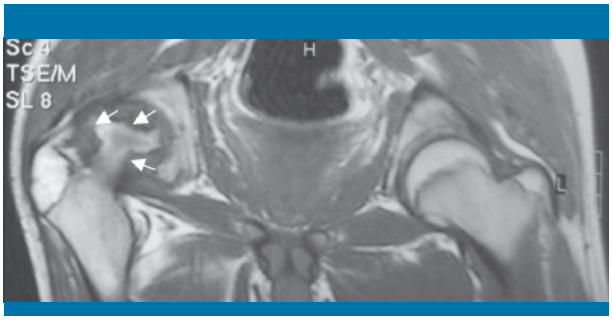

Figure 4. (b) *T1 coronal MRI showing deformed right femoral head with marked cortical erosions. Moderate synovial hypertrophy (arrows) and minimal hemosiderin deposition in the form of dark signal intensity shown by (small arrows)*

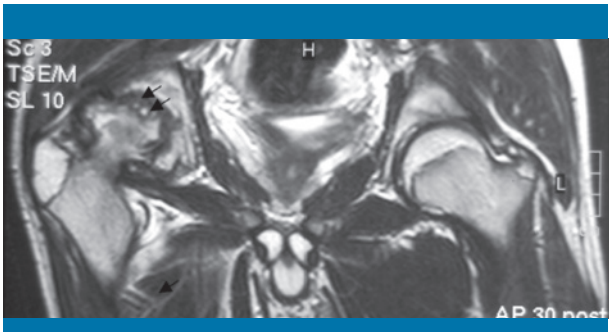

Figure 4. (c) *Multiple subchondral cysts of intermediate T1 weighted and bright T2 weighted images signal intensities are also seen (black arrows)*

most cases. On radiological evaluation of seventeen asymptomatic joints their scores ranged from 0 to 2 and in only 3 patients it ranged from 3 to 5.

On MRI evaluation of 17 joints by the Denver and European scores, they showed a wide range of abnormalities. The MRI score ranged from 1 to 11 with a mean of 4.0 (intrequartile, 2.5-7.0). Cysts and/or erosions were the main MRI findings in 12/17, 70.6% (figures 1b, 3, 4c). Eight patients (47.1%) showed synovial hypertrophy and/or hemosiderin deposits. Nearly all joints showed minimal effusion but the effusion was moderate to severe in 6/17 (35.3%) (figures 1c, 3, 4b). Several joints with history of hemarthrosis were found with hemosiderin deposition but no synovial hypertrophy. Also, some joints though showing cartilage loss, which was only mild or no synovial hypertrophy.

Correlation of the clinical score with the X-ray was non- significant but that with the Denver MRI score was significant (r= 0.5, p= 0.04*) as well as that of the plain X-ray and Denver score (r= 0.5, p= 0.05*).

The correlation of number of joint bleeds per year with the clinical score was non- significant but it was significant with the plain X-ray scale (r= 0.5, p= 0.01*) and MRI score (r= 0.6, p= 0.02*) (figures 5, 6). In four joints with a history of ≤ 3 bleeds/year in the past 2 years the clinical, radiological as well as the MRI scores showed mild changes. Only one joint had a clinical score of 8 but this is a16-year old with severe Hemophilia A who used to have more frequent bleeds and now nearly stopped having joint bleeds and started having muscle bleeds and his radiological and MRI scoring is 3 and 8 respectively.

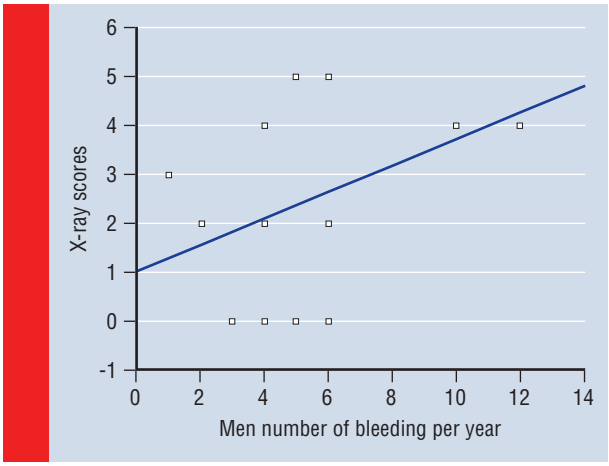

Figure 5. *Correlation between mean number of joint bleeds per year and X-ray scores of hemophilic patients (r= 0.5, p= 0.01*)*

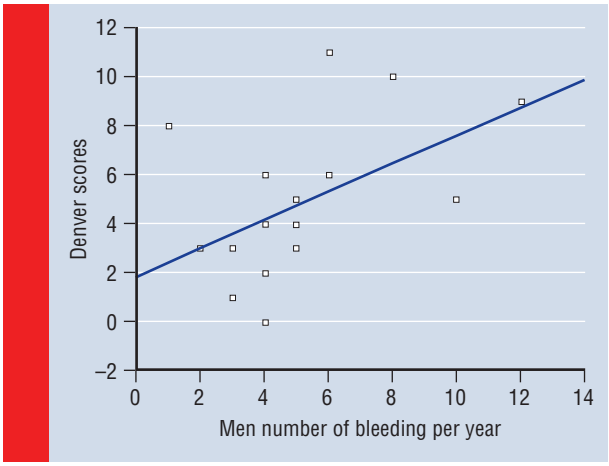

Figure 6. *Correlation between mean number of joint bleeds per year and Denver MRI scores of hemophilic patients (r= 0.6, p= 0.02*)*

The rest of the joints with history of four or more bleeds had moderate to severe changes on plain radiography and MRI evaluation.

Discussion

Hemophilic arthropathy, the result of recurrent hemorrhages in the same joint, remains a major concern for physicians, patients and their families, as it affects patient's quality of life and the overall cost of hemophilic management.[4]

Of the methods used for evaluation of hemophilic arthropathy is the clinical joint assessment. Though scoring is easy to perform and has no cost yet it can only detect advanced arthropathy expressed as an impairment of the joint function. The optimal clinical method for assessing the joint is a subject of concern among experts for several reasons.[19,20] In our study, clinical evaluation was done using the physical examination score of the Orthopedic Committee of the WFH.[6] Correlation of the clinical score of our patients with the Arnold Hilgartner radiological score was non- significant but the one with the MRI score was significant (r= 0.6, p= 0.02).Other studies showed that the clinical score did not correlate with the MRI findings[4,14] though in the latter study it was evaluated with the more detailed WFH, PE scoring system.[21] However, their patient group showed no abnormality on clinical evaluation in 55.4% as opposed to 7.7% in our group but 62.5% of their patients was on prophylaxis treatment whereas none of our patients were.

It has been recently suggested that the physical examination score proposed by the WFH was initially designed for the assessment of joint damage in adults over 20 years and so is not sensitive enough for the orthopedic evaluation of joint status in hemophilic children especially in the early stages. Therefore additional features have been suggested to be applied in children from 12 months of age for the correct physical examination assessment of orthopedic status during childhood and puberty.[19] Though physical findings may be indicative of joint alterations they are not always diagnostic during childhood. Moreover, even if specified criteria is used, it would be difficult to quantify swelling, atrophy and crepitus on motion as evaluation of these features is subjective.[19]

Conventional radiography has been the only radiological method for assessment of the joint damage for almost 3 decades;[22] however it does not provide evidence of the earliest abnormalities, as well as correct evaluation of the synovial membrane or the articular cartilage which are the target tissues where initial damage to the joint is developed.[9] This agrees with our study where 18 joints assessed by Arnold Hilgartner had a score between 2.0 and 5.0 but showed more profound alterations on MRI. Although no abnormality was detected in seven joints (44.4%) yet 6/7 (85.7%) showed some changes when further assessed by the MRI. This agrees with other studies where 34.3% had zero Pettersson radiological score but 50% showed alterations on MRI evaluation.[4] Also, some authors reported that 66.6% of patients showed no arthropathic changes by Pettersson score in joints with history of 3 bleeds whereas the MRI showed initial alterations.[12]

So, plain X-ray films can only partially reveal early arthropathic signs and physical examination reveals clinical dysfunction in joints with more than 3 bleeds. Accordingly, physical examination and radiology are less sensitive for the detection of the first signs of hemophilic arthropathy as compared with MRI.[23, 24]

Some authors found normal functioning only in joints with less than three bleeds.[25] In view of this finding and that the radiological assessment of the major joints require, considerable radiation exposure providing little information it was recommended to avoid, radiological screening of joints with less than three bleeds.[12] However, with radiological evaluation done on seventeen asymptomatic joints, our patient group scores ranged

from 0 to 2 and even in 3 patients it ranged from 3 to 5. So, our findings suggest that the presence of an ongoing process of hemophilic arthropathy begins before the joints become symptomatic.[14,26] Subclinical bleeding in the joints may have triggered early joint damage in joints which have not suffered from any clinically evident joint bleeds yet.[8]

The MRI seems to provide a better resolution and enables the detection of early stages of hemophilic arthropathy as well as unmasks more advanced changes in the cartilage or bone than those detected by a plain radiography.[10,14,27,28] In our study, MRI evaluation of 17 joints by the Denver and European scores, showed a wide range of abnormalities; cysts and/or erosions in 70.6%, synovial hypertrophy and/or hemosiderin deposition in 47.1% and moderate to severe effusion in 35.3%. In some studies synovial hypertrophy and/or hemosiderin deposition were the main findings followed by cysts and/or erosions in 66.6% of affected joints.[4]

There is a conflict in theories expressed by several investigators as regards to the order of events towards the development of arthritic changes. In our study, several joints with history of hemarthrosis had hemosiderin deposits without synovial hypertrophy. Also, some joints though showing cartilage loss showed only mild or no synovial hypertrophy. It was stated that synovial hypertrophy was not found in all joints with cartilage loss in early stage of arthropathy.[12] This can be attributed to the non- chronological appearance of alterations of the synovium and cartilage damage in some cases.[29,30]

Four patients had an X-ray score of 2 but when assessed by the MRI had scores of 1, 3, 4 and 10 respectively. Those with scores ≥3 by Arnold Hilgartner had MRI scoring ranging from 4-11 with synovial hypertrophy in most cases. This is in agreement with what other authors stated that Arnold Hilgartner scoring allows a good prediction of synovial hypertrophy in knee and ankle joints and suggested that whenever the Arnold Hilgartner is ≥ 3 we can proceed to MRI for confirmation.[26]

The number of joint bleeds is a crucial factor for the appearance of hemophilic arthropathy. In our study, it correlated significantly with plain X-ray (r= 0.5, p= 0.01*) and MRI scores (r= 0.6, p= 0.02*) but not with the clinical score. This is in agreement with some authors who showed that correlation of the number of hemorrhages per joint per year was satisfactory with the Denver MRI score as well as the Pettersson radiological score but not the clinical one.[4] Also, in some studies, despite the small number of investigated patients yet the degree of hemophilic arthropathy correlated well with the number of joint bleeds (p= <0.001*).[12]

Numerous publications showed that the intensity of radiological changes increased with the patients' age.[31-33] In our study, many older patients showed more changes than younger ones though no significant correlation was found between the age of patients and the clinical, radiological or the MRI scoring.

However, patients 11 and 14 who are 9 and 14 years old respectively showed clinical and radiological findings similar to those of much younger patients. Patient 11 who is 9-years old though severe is behaving phenotypically as mild and showed mild changes both on plain X-ray and MRI. This agrees with some studies which showed that the disease may take a different course inspite of FVIII or FIX deficiency indicating a severe type of hemophilia.[35] Not infrequently young children suffer from recurrent joint bleeds with signs of hemophilic arthropathy, whereas teenagers present with normal joints. There are without doubt other reasons for this apart from the level of deficient coagulation factors such as defects of stature, structure of the myoligamentous system, circumstances and dimension of the first intra-articular bleeding, the method of treatment, the time of recurrence of bleeding into the same joint and proper physiotherapy.[5,35] Also, the degree of intensity of joint changes is dependent on the length of time that the blood is retained in the joint, the chronicity of synovitis, the time of bleeding recurrence in relation to the phase of previous bleeding episodes, the dimension of hemarthrosis and the time of starting hemostatic treatment.[36]

From our results neither the presence of symptomatology nor radiographic findings can be used to replace MRI in the detection of synovial hypertrophy which is in agreement with previous studies.[14,27,28]

In conclusion, MRI is a sensitive diagnostic tool in documenting early arthritic changes in hemophilic children with no obvious clinical signs of arthropathy. Besides, it can unmask more advanced arthritic alterations than those detected by conventional radiography. In view of the resource constraint, MRI can play an important role in staging patients for appropriate treatment of hemophilic joint disease. It can tell if there's active bleeding in the joint, chronic synovitis and synovial hypertrophy, effusion or fibrosis with a contracted joint. However, the only option to prevent all these joint problems is by minimizing joint bleeds and starting patients on long term prophylaxis with FVIII or FIX concentrates.

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