EJR European Journal of Rheumatology

DOI: 10.5152/eurjrheum.2019.19040

Original Article

Joint scores in hemophilic arthropathy in children: Developing country perspectives

Aritra Guha[1], Akash Rai[1], Arnab Nandy[1], Tanushree Mondal[2], Narayan Pandit[3], Sumantra Guha[4], Dipankar Gupta[1], Rakesh Mondal[1]

Abstract

Objective: Hemophilia is a common X-linked recessive coagulopathy causing recurrent bleeding into the synovial joints and results in articular and periarticular abnormalities. To our knowledge, this is the first comprehensive study aimed at studying the clinico-radiological joint score evaluation in hemophilic arthropathy in children from a developing country and its possible impact on the quality of life.

Methods: In this hospital-based, prospective, descriptive study, all children presenting to the pediatric rheumatology clinic were studied. The joint physical examination was scored using the Hemophilia Joint Health Score 2.1 (HJHS 2.1). The patients were then subjected to imaging of the most affected joint using ultrasonography (USG) and magnetic resonance imaging (MRI). Detailed USG and MRI radiological evaluation was recorded in the predesigned proforma using the Hemophilia Early Arthropathy Detection with Ultra Sound (HEAD-US) score and MRI DENVER score. The physical quality of life as per Functional Independence Score in Hemophilia (FISH) was noted. The clinical, radiological, and functional scores were analyzed with an appropriate statistical measure.

Results: The mean age at presentation was 7.4 years (interquartile range 4.9-10), with the knee being the most common joint involved. All of the USG score, MRI score, and FISH score have a significant correlation ($p<0.05$), with the HJHS 2.1 score with correlation coefficients of 0.7086, −0.8916, and 0.8607, respectively. USG and MRI had a correlation coefficient of −0.7145 and −0.8326 with FISH, respectively.

Conclusion: The degree of association between HJHS 2.1 score was found to be maximum with HEAD-US score, whereas a negative correlation was seen evaluating FISH score with both HEAD-US and MRI DENVER scores. Use of these scores, specifically HEAD-US score, will result in consistent assessment of hemophilic joints, optimizing the management of the destructive changes.

Keywords: Hemophilia, arthropathy, degenerative arthropathy, quality of life

ORCID IDs of the authors:
A.G. 0000-0002-7798-4728;
A.R. 0000-0002-6666-7663;
A.N. 0000-0002-7075-1040;
T.M. 0000-0002-2727-3354;
N.P. 0000-0003-1466-3481;
S.G. 0000-0002-9867-7065;
R.M. 0000-0002-2241-3514.

Cite this article as: Guha A, Rai A, Nandy A, Mondal T, Pandit N, Guha S, et al. Joint scores in hemophilic arthropathy in children: Developing country perspectives. Eur J Rheumatol 2020; 7(1): 26-30.

[1] Pediatric Rheumatology Clinic, Department of Pediatric Medicine, North Bengal Medical College, Darjeeling, India
[2] Department of Community Medicine, Medical College, Kolkata, India
[3] Department of Radiodiagnosis, Coochbehar Govt. Medical College, Coochbehar, India
[4] IFMR graduate School of Business, KREA University, Chennai, India

Address for Correspondence: Rakesh Mondal; Pediatric Rheumatology Clinic, Department of Pediatric Medicine, North Bengal Medical College, Darjeeling, India

E-mail: ivanrakesh2001@gmail.com

Submitted: February 26, 2019
Accepted: September 9, 2019
Available Online Date: December 16, 2019

Introduction

Hemophilic arthropathy (HA), a crippling joint disease, leads to severe disability often necessitating joint replacement (1-3). Arthropathy continues to be the most common complication of hemophilia (4-6) despite attempts to prevent bleeding by substitution therapy with the missing clotting factors (7, 8). Knee, ankle, elbow, shoulder, and hip are the joints usually affected in descending order of frequency (9). Early findings include hemarthrosis and joint effusion, followed by articular and periarticular changes (including hemosiderin deposition and synovial hypertrophy). The later stages, as a result of hyperemia, exhibit osteopenia and epiphyseal overgrowth, destructive changes, such as loss of cartilage, along with early closure of physeal plate, bone erosions, and subchondral cyst formation (10, 11). Studies suggest that hemophilic arthropathy is a multifactorial event (12), including both inflammatory synovium-mediated and degenerative cartilage-mediated components (13). The early stages of HA have some similarities with arthritides, such as rheumatoid arthritis, whereas the later degenerative stages of HA have certain features in common with osteoarthritis (14). Most of the arthritis commonly encountered among the pediatric population is inflammatory in nature. Thus, HA presents as one of the rare models of degenerative arthropathy in children. Being a resource-limited country, most of the children with HA in our set-ups are on "on-demand" clotting factor substitution therapy. Thus, the joint damage in these patients in most cases tends to be quite extensive. However, the joint damage in HA and its impact on the quality of life is not well studied, and there is a definite paucity of data from developing countries. To the best of our knowledge, this is the first comprehensive study aimed at studying HA as a model of degenerative arthropathy in children from developing countries. The aim of the present study was to describe the clinico-radiological joint score evaluation of HA and its possible impact on the quality of life.

Methods

Study design

This was a hospital-based, prospective, descriptive study to assess all children presenting with hemophiliac arthropathy over 1 year.

Patient recruitment

Inclusion criteria consisted of children aged 1-12 years, diagnosed with hemophilia A or B, who presented to the pediatric rheumatology clinic with permanent joint damage as a long-term consequence of repeated hemarthrosis and at the Department of Pediatrics, North Bengal Medical College, Darjeeling, West Bengal, India with HA or history of HA from February 2018 to January 2019. Prior to assessments, parents of children with hemophilia were informed of the objectives of the study, and they signed an informed consent document. The study was approved by the Institutional Ethics Committee.

Evaluations

A detailed history was collected, and the joint physical examination was scored using the Hemophilia Joint Health Score 2.1 (HJHS 2.1). The patients were then subjected to imaging of the most affected joint using ultrasonography (USG) and magnetic resonance imaging (MRI). USG was performed using GE LOGIQ F8 (8-10 MHz high frequency), and MRI was done using predominantly the T2-weighted sequence with a BRAVO Model 1.5 Tesla MRI (GE make) under the guidance of a radiologist. The USG and MRI evaluation was recorded in the predesigned proforma using the Hemophilia Early Arthropathy Detection with Ultra Sound (HEAD-US) score and MRI DENVER score. The physical quality of life as per Functional Independence Score in Hemophilia (FISH) was also recorded.

Descriptive statistics were performed to calculate the mean, standard deviation, median, interquartile range (IQR), and percentage. Correlation coefficient has been computed between variables taking two at a time. Pearson's correlation formula was applied. Simple linear regression model has been applied as dependent and independent variables. A p-value<0.05 was considered to be statistically significant.

The HJHS 2.1 is used for an objective observation of clinical changes in joints due to the development of HA. This scale consists of eight items per joint (plus gait analyzed globally), and evaluates the following: (1) joint swelling, (2) duration of swelling, (3) muscle atrophy, (4) strength, (5) crepitus on motion, (6) flexion loss, (7) extension loss, and (8) pain. The full range of score for the updated HJHS 2.1 is from 0 to 124 points (0-20 points for each of the six evaluated joints, plus 4 points for the overall assessment of gait).[15]

The HEAD-US method estimates joint disease activity by the presence of synovial hypertrophy and joint damage by looking at the cartilage and the bone and the presence of prominent osteophytes around the joint (16). The full range of score is from 0 to 8 points.

The MRI Denver score is a progressive score in which different stages of the pathology are classified in relation to the most severe finding and assigned a score (maximum score of 10) (17).

The FISH assesses seven daily activities of the patients, and the patient is scored 1-4 for each activity based on his ability to perform the activity or lack of it. The total score ranges from 7 to 28 (18).

Main Points

- Haemophilic arthropathy is a multifactorial event having both inflammatory synovium-mediated as well as degenerative cartilage-mediated components.
- This comprehensive study aimed at studying hemophilic arthropathy as a proto-type of mechanical and degenerative arthropathy in children.
- Various radiological and functional scores are available for the assessment of the extent of joint disease in children.
- A quick and affordable technique, ultrasound imaging of joints emerges as efficient and reliable tool for early detection of hemophilic arthropathy.
- Use of HEAD-US score will result in consistent assessment of hemophilic joints and facilitate development of targeted treatment to prevent the destructive changes in the articular cartilage.

Results

The mean age at presentation is 7.4 years (IQR 4.9-10). Of a total of 30 participants, 21 had hemophilia A and 9 had hemophilia B. The ages at presentation were 7.7 years (IQR 5.3-10.5) for hemophilia A and 6.7 years (IQR 3.8-9.5) for hemophilia B. However, as the two are similar in their clinical presentation and imaging findings (11), we did not study them as separate entities. Only three children were on weekly prophylaxis, and the rest of the children were on on-demand clotting factor replacement. Our study revealed the knee (50%) to be most commonly involved joint, followed by the elbow and ankle. The clinical characteristics of these patients are depicted in Table 1.

Figure 1 shows the study flow diagram of the approach followed for the evaluation of these patients with HA.

The scores obtained from the HJHS 2.1, the HEAD-US score, the MRI DENVER score, and the FISH are compiled in Table 2.

HEAD-US score was found to have a significant correlation with duration of disease, but MRI Denver score, FISH, and HJHS 2.1 were found to be not statistically significant when equated with the same.

We studied the HJHS 2.1 as a predictor of HEAD-US score, MRI Denver score, and FISH score using similar correlation coefficient and regression statistics. Here all three data were statistically significant (p<0.05). HJHS 2.1 score when compared with HEAD-US score (R^2 0.50) (Figure 2), MRI Denver score, and FISH score gave correlation coefficients of 0.7086, −0.8916, and 0.8607, respectively.

Table 1. Characteristics of patients with hemophilic arthropathy (n=30).

Variable	n (%)	Mean (IQR)
Type		
Hemophilia A	21 (70)	-
Hemophilia B	9 (30)	-
Age at presentation		
Hemophilia A	-	7.7 years (IQR: 5.3-10.5)
Hemophilia B	-	6.7 years (IQR: 3.8-9.5)
Duration of disease		
Hemophilia A	-	5.8 years (IQR: 3-8.8)
Hemophilia B	-	5.0 years (IQR: 2.5-7.5)
Factor replacement		
On demand	27 (90)	-
Prophylaxis	3 (10)	-
Joint involved		
Knee	15 (50)	-
Elbow	9 (30)	-
Ankle	6 (20)	-

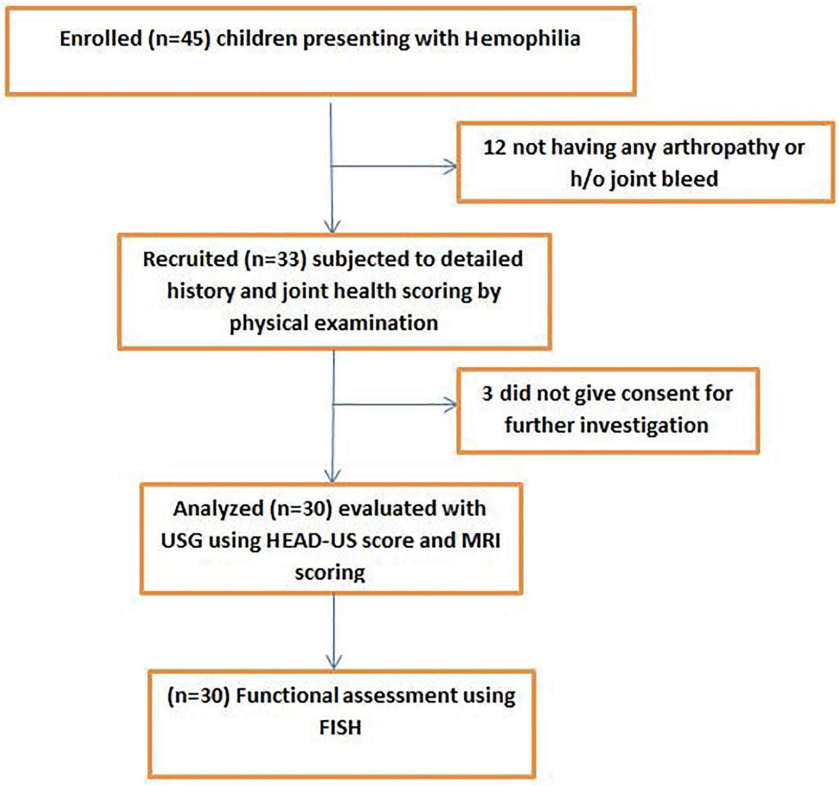

Figure 1. Study flow diagram.

Table 2. Joint scores compiled from patients (n=30).

Score	Parameter studied	Maximum value	Minimum value	Mean	SD	IQR
HJHS 2.1*	Physical examination	28	4	17.76	8.74	8.75-27
HEAD-US**	Radiological	5	0	2.23	1.48	1-3.5
MRI DENVER#	Radiological	8	1	4.53	2.16	2-7
FISH¶	Functional assessment	28	13	18.93	4.43	15.75-23

*Hemophilia Joint Health Score 2.1.
**Hemophilia Early Arthropathy Detection with Ultra Sound.
#MRI DENVER score.
¶Functional Independence Score for Hemophilia.

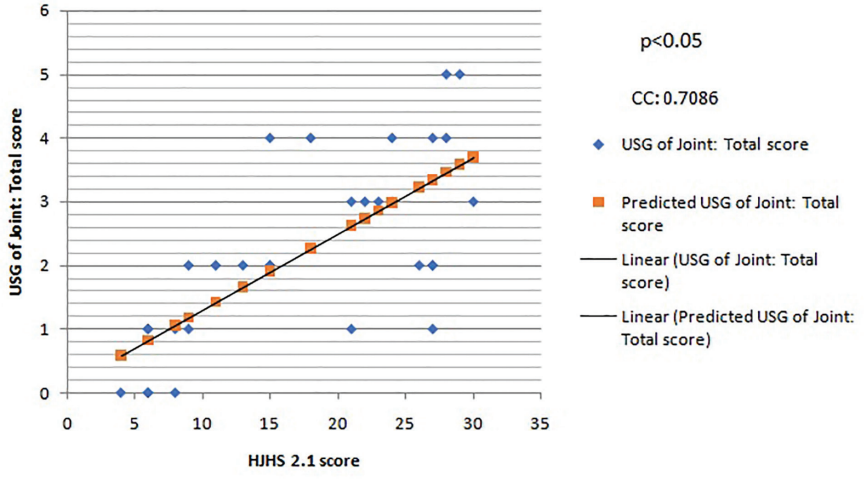

Figure 2. Scatter plot of HJHS 2.1 score with HEAD-US score.

HEAD-US score versus FISH score had a correlation coefficient (r=–0.714) suggesting a 71.4% degree of association between FISH and HEAD-US score as depicted in Figure 3. In comparison, Figure 4 (R^2 0.69) shows that MRI Denver score when equated with FISH score had a correlation coefficient of (–) 0.83.

Discussion

Bleeding frequency is the most important clinical endpoints used to assess the efficacy of hemophilia treatments (19). A dramatic reduction in the incidence of joint bleeds and arthropathy was shown in patients on prophylaxis by Nilsson et al (20). However, our study conducted on episodic therapy compares the degree of association between the joint health score and the HEAD-US score, MRI Denver score, and FISH. We found that the degree of association between HJHS 2.1 score was at maximum with HEAD-US score, whereas a negative correlation could be established while evaluating FISH score with both HEAD-US and MRI DENVER scores. Thus, this highlights the importance of USG in the assessment and monitoring of the "target" joint. It also makes USG the most efficient tool for the early detection of arthropathy.

In the recent Indonesian study by Sari et al., they found that the joint outcome of children with severe hemophilia A who were receiving episodic treatment evaluated by HJHS and HEAD-US scoring shows more severe damage in older than in younger ones (21). Altisent et al. (22) utilized HJHS and HEAD-US scores in children with severe hemophilia treated with clotting factor prophylaxis and found that HJHS and HEAD-US scores are concordant in 91/124 (73.4%) joints. Thus, they inferred that USG with HEAD-US method detected a higher percentage of abnormalities than physical evaluation. Our study in comparison showed a 50% positive correlation between HJHS 2.1 and HEAD-US scores.

In another Iranian cross-sectional study by Tasbihi et al. on 25 patients with severe hemophilia, FISH, MRI, and sonography procedures were performed. They found a statistically significant negative correlation between FISH and MRI Additive (A) scale (r_s=–0.537, p=0.006) (23). Our study also similarly showed a negative correlation between FISH and HEAD-US and MRI DENVER score.

Even objective joint assessment similar to the indexed study is useful for the evaluation of patients with hemophilic joint disease on early prophylaxis as reported by Fischer et al. (24).

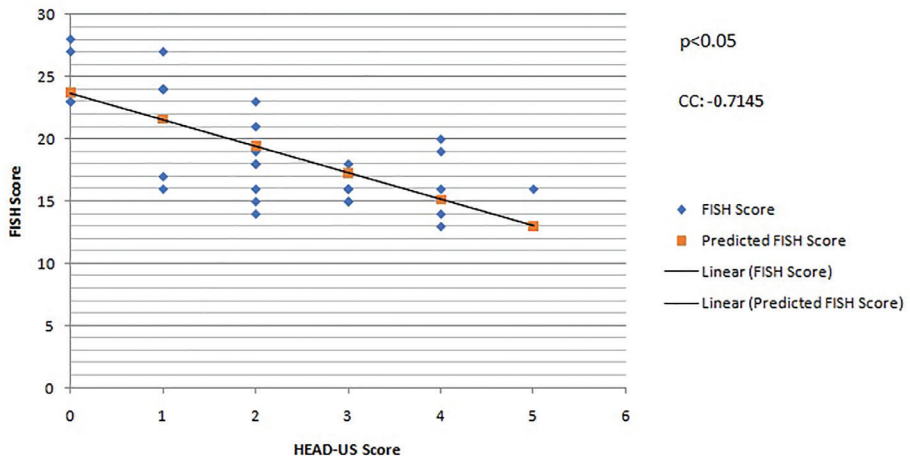

Figure 3. Scatter plot of HEAD-US score with FISH score.

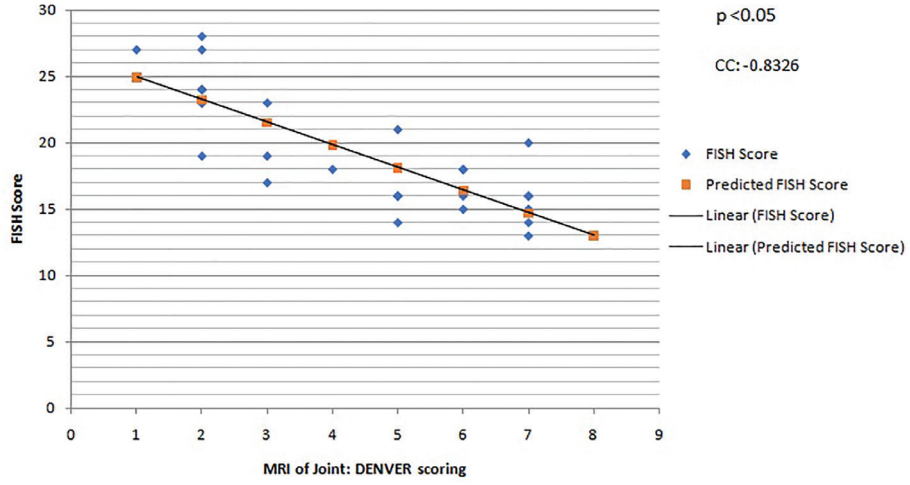

Figure 4. Scatter plot of MRI DENVER score with FISH score.

To the best of our knowledge, this is the first comprehensive study that compiles all relevant scores across clinico-radiological evaluation of HA as a model of mechanical and degenerative arthropathy in the pediatric population.

Our study has limitations. This was a hospital-based study with a small sample size. Majority of the patients were on episodic factor replacement as compared with prophylaxis, so we have not analyzed separately the relationship of therapeutic practice in our study. The lack of follow-up data for the re-evaluation of the patients hindered a better understanding of the disease process and its impact.

Further multicentric community-based study of joint scores in HA (both prophylaxis and episodic) in larger population is warranted for the in-depth assessment of joint damage and its impact.

In conclusion, the degree of association between HJHS 2.1 score was found to be maximum with HEAD-US score, whereas a negative correlation could be established while evaluating FISH score with both HEAD-US and MRI DENVER scores. USG emerges as the most efficient tool for the early detection of arthropathy, and the HEAD-US score can be used for the consistent assessment of hemophilic joints optimizing the management of the destructive changes.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of North Bengal Medical College.

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - A.G., A.R., A.N., T.M., N.P., S.G., D.G., R.M.; Design - A.G., A.R., A.N., T.M., N.P., S.G., D.G., R.M.; Supervision - A.G., A.R., A.N., T.M., N.P., S.G., D.G., R.M.; Data Collection and/or Processing - A.R., A.N., N.P.; Analysis and/or Interpretation - S.G., D.G., A.G., R.M.; Literature Search - T.M., A.G., R.M.; Writing Manuscript - A.G., R.M., T.M., A.n.; Critical Review - A.G., R.M., N.P., D.G., S.G.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

References

1. Roosendaal, Rinsum V, Vianen, Berg VD, Lafeber, Bijlsma. Haemophilic arthropathy resembles degenerative rather than inflammatory joint disease. Histopathology 1999; 34: 144-53. **[CrossRef]**
2. Arnold WD, Hilgartner MW. Haemophilic arthropathy. Current concepts of pathogenesis and management. J Bone Joint Surg 1977; 59; 287-305. **[CrossRef]**
3. Madhok R, York J, Sturrock RD. Haemophilic arthritis. Ann Rheum Dis 1991; 50; 588-91. **[CrossRef]**
4. Aledort LM, Haschmeyer RH, Pettersson H. A longitudinal study of orthopaedic outcomes for severe factor-VIII-deficient haemophiliacs. The Orthopaedic Outcome Study Group. J Int Med 1994; 236; 391-9. **[CrossRef]**
5. Petrini P, Lindvall N, Egberg N, Blomback M. Prophylaxis withfactor concentrates in preventing haemophilic arthropathy. Am J Ped Hematol Oncol 1991; 13; 280-7. **[CrossRef]**
6. Soreff J, Blomback M. Arthropathy in children with severehemophilia A. Acta Paedriatr Scand 1980; 69; 667-73. **[CrossRef]**
7. Lusher JM. Considerations for recurrent and future management of haemophilia and its complications. Haemophilia 1995; 1; 2-10. **[CrossRef]**
8. Nilsson IM, Bertorp E, Lofqvist T, Pettersson H. Twenty-five years' experience of prophylactic treatment in severe haemophilia A and B. J Int Med 1992; 232; 25-32. **[CrossRef]**
9. Resnick D. Diagnosis of Bone and Joint Disorders, 4th edn. Philadelphia, PA: WB Saunders; 2002.
10. Berquist TH. MR imaging of the musculoskeletal system, 5thedn. In: Elbow and Forearm. Philadelphia, PA: Lippincott Williams & Wilkins, 2006. p. 708-9.
11. Jaganathan S, Gamanagatti S, Goyal A. Musculoskeletal Manifestations of Hemophilia: Imaging Features. Cur Prob Diagn Radiol 2011; 40: 191-7. **[CrossRef]**
12. Valentino LA, Hakobyan N, Rodriguez N, Hoots WK. Pathogenesis of haemophilic synovitis: experimental studies on blood-induced joint damage. Haemophilia 2007; 13 (Suppl 3): 10-3. **[CrossRef]**
13. Roosendaal G, Lafeber FP. Pathogenesis of haemophilic arthropathy. Haemophilia. 2006; 12: 117-21. **[CrossRef]**
14. Haxaire C, Kalliolias G, Dicarlo E, Salmon J, Srivastava A, Blobel C. Blood-Induced Arthropathy in Hemophilia: Mechanisms and Heterogeneity. Semin Thromb Hemost 2015; 41: 832-7. **[CrossRef]**

15. Bladen M, Main E, Hubert N, Koutoumanou E, Liesner R, Khair K. Factors affecting the Haemophilia Joint Health Score in children with severe haemophilia. Haemophilia 2013; 19: 626-31. **[CrossRef]**
16. Martinoli Carlo, Alberighi Ornella Della Casa, Di MinnoGiovanni, GrazianoErmelinda, Molinari Angelo Claudio,Pasta Gianluigi, et al. Development and definition of asimplified scanning procedure and scoring method forHaemophilia Early Arthropathy Detection with Ultrasound(-HEAD-US). J Thromb Haemost 2013; 109: 1170-9. **[CrossRef]**
17. Abdelwahab M, Elsayed N. Radiological and clinical evaluation of hemophilic arthropathy in Egyptian patients. Acta Pediatr Esp 2010; 68: 71-8.
18. Poonnoose PM, Manigandan C, Thomas R, Shyamkumar NK, Kavitha ML, Bhattacharji S, et al. Functional Independence Score in Haemophilia: a new performance-based instrument to measure disability. Haemophilia 2005; 11: 598-602. **[CrossRef]**
19. Chai-Adisaksopha C, Hillis C, Thabane L, Iorio A. A systematic review of definitions and reporting of bleeding outcome measures in haemophilia. Haemophilia 2015; 21: 731-5. **[CrossRef]**
20. Nilsson IM, Berntorp E, Löfqvist T, Pettersson H. Twenty-five years' experience of prophylactic treatment in severe haemophilia A and B. J Intern Med 1992; 232: 25-32. **[CrossRef]**
21. Sari TT, Chozie NA, Gatot D, Tulaar AB, Dharma R, Sukrisman L, et al. Clinical and ultrasound joint outcomes in severe hemophilia A children receiving episodic treatment in Indonesian National Hemophilia Treatment Center. Med J Indones 2017; 26: 47. **[CrossRef]**
22. Altisent C, Martorell M, Crespo A, Casas L, Torrents C, Parra R. Early prophylaxis in children with severe haemophilia A: clinical and ultrasound imaging outcomes. Haemophilia 2015; 22: 218-24. **[CrossRef]**
23. Tasbihi M, Pishdad P, Haghpanah S, Ardeshiri R, Tavoosi H, Karimi M. A comparison between MRI, sonography and Functional Independence Score in Haemophilia methods in diagnosis, evaluation and classification of arthropathy in severe haemophilia A and B. Blood Coagul Fibrinolysis 2016; 27: 131-5. **[CrossRef]**
24. Fischer K, Nijdam A, Holmström M, Petrini P, Ljung R, Schouw YTVD, et al. Evaluating outcome of prophylaxis in haemophilia: objective and self-reported instruments should be combined. Haemophilia 2016; 22: e80-6. **[CrossRef]**