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Assessment of Joint Health Status of Haemophilia Patients in a Tertiary Care Hospital of Bangladesh

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ABSTRACT

Background: *Haemophilia is a sex-linked bleeding disorder resulting from deficiency of clotting factor VIII or IX. Affected patients suffer spontaneous or post-traumatic bleeding into various sites of the body, mainly into joints, depending on the level of coagulation factor deficiency. Recurrent joint bleeds lead to progressive disability. Susceptibility to joint haemorrhage in persons with haemophilia suggests that the routine assessment of joint health is an important aspect of clinical management and outcome assessing the efficacy of treatment. The aim of this study was to assess joint health status in haemophilia patients attending a tertiary care hospital, Bangladesh.* ***Methodology:*** *A descriptive observational study was carried out in the department of Haematology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. A total number of 45 patients who attended outpatient department and got admitted into the hospital, meeting inclusion and exclusion criteria were included in the study. Joint assessment was done according to the Haemophilia Joint Health Score (HJHS) version2.1. Clinical and laboratory information was recorded with a semi structured questionnaire.* ***Result:*** *Among 45 haemophilia patients, the mean age was 12.9±3.4 years while males were predominant (91.1%). Majority (80.0%) of the patients (36) were diagnosed as haemophilia A. This study observed that, 48.9% of the patients had moderate and 28.9% had severe haemophilia. Knee joint was the predominant target joint. Left knee joint involved in 80% cases and right knee joint were involved in 55.6% of patients. The mean global gait score was found 1.49±0.66 and mean HJHS score was 15.8±4.4. There was no significant correlation between HJHS score and severity of haemophilia (r= -0.081; p=0.596) while significant correlations between the ages of patient with HJHS score (r=0.536; p=0.001) was observed.* ***Conclusion:*** *Haemophilia is a debilitating and life-threatening disease that affects mostly knee, ankle and elbow joints. The joint evaluation system is of paramount importance in clinical practice which is capable of preventing major haemarthrosis and chronic haemophilic synovitis. Haemophilia Joint Health Score (HJHS) is an effective and reliable tool to detect early and subtle changes in joint health and function. This study finding will help in future to assess the joint conditions and complications early, which will assist to modify the treatment approach in individual patients.*

Key words: *Haemophilia, Haemophilia Joint Health Score (HJHS).*

Introduction

Haemophilia A and B are X-linked recessive bleeding disorders caused by defective factor VIII (FVIII) and factor IX (FIX) genes which affect approximately 1 in 5,000 and 30,000 live births, respectively, in the general population.[1] Both factors take part in the intrinsic pathway of blood coagulation and the clinical pictures are indistinguishable. Affected individuals have severe, moderate and mild forms of the diseases, defined by factor plasma levels of 1% or less, 1 to 5% and 6 to 40%, respectively.[2] The disease manifests in the severe and moderate forms as bleeding into the joints (hemarthrosis), soft tissues, and muscles after minor trauma or even spontaneously, and in the mild form as infrequent bleeding that is usually secondary to trauma.

In haemophilia, the most affected joints, are the knees (accounting for one half of all haemarthroses), elbows and ankles.[3] Less commonly bleeding occurs into multi-axial joints: shoulders, wrists, hips. Repeated haemarthrosis leads to the development of target joints (defined as a single joint that has experienced three or more bleeds in a consecutive three-month period).[4]

The mechanism of Haemophilic Arthropathy (HA) is multifactorial; joint bleeds affect cartilage directly and indirectly through synovial inflammation. HA leads to pain, loss of range of motion and muscle atrophy resulting in loss of activities.[5]

Severity of disease, use of prophylactic clotting factors replacement, number of joint bleeds, radiological status, synovitis and Body Mass Index (BMI) etc. are the known factors related to joint health in haemophilia.

There is evidence that initiation of prophylactic clotting factor treatment in early childhood (age <2 years) and higher intensity dosing regimens has beneficial effects on joint outcomes. HA cannot be entirely avoided, as shown by a high percentage of adults with haemophilia from industrialized countries (approx. 30-50% of patients) presenting with clinical arthropathy despite access to prophylaxis since childhood.[6]

The Haemophilia Joint Health Score (HJHS) was developed by the International Prophylaxis Study Group in 2002 for evaluation of joint function in paediatric patients with haemophilia.[3] Based on expert review of existing measures and consensus of the most relevant items, the HJHS is an 11-item scoring tool for assessing joint impairments of the six index joints in boys with haemophilia aged 4-18 years.

Haemophilic arthropathy is a disabling condition characterized by joint impairment, chronic pain, and reduced quality of life. Early assessment of joint deformity or deterioration can save the limbs and movement as well. Till date, there are very limited literatures and studies available on this topic in Bangladesh. Therefore, this study was done to assess joint health status of haemophilia patients in a tertiary care hospital of this country.

Material and Methods

This was a descriptive cross-sectional study which was done at the Department of Haematology of Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh within a study period from December 2018 to November 2019. Study population was covered from both indoor and outdoor patients of Haemophilia (ageing 4 to 18 years) attending the department of haematology. The patients' clinical features consistent with haemophilia were screened based on the history, clinical examination and by laboratory test. After that, patients and parents of the patients were approached to participate into the study. During enrolment, inclusion and exclusion criteria were matched for each individual. Ethical issues were addressed to

every patient. Special precaution was taken to personal history. Ethical clearance was obtained from institutional review board (IRB) of BSMMU.

Results

This descriptive cross-sectional study was carried out with the aim to assess the joint health status among the haemophilia patients. A total of 45 Haemophilia patients were enrolled for the study. Among them 10 patients were mild, 22 patients were moderate, and 13 patients were severe haemophiliacs. (Figure 1)

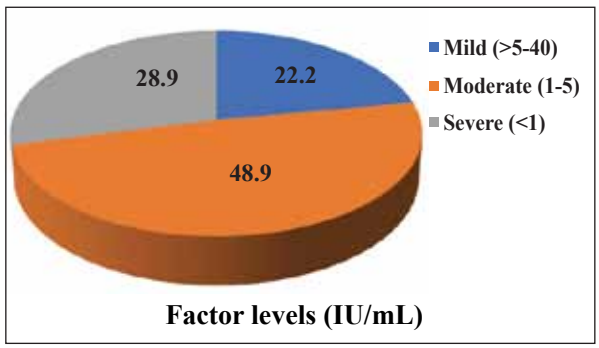

Figure 1. Pie chart showing factor levels (severity of haemophilia) of the study patients (n=45)

Among the 45 patients left knee joints were found to be affected most, followed right knee joints (Figure 2)

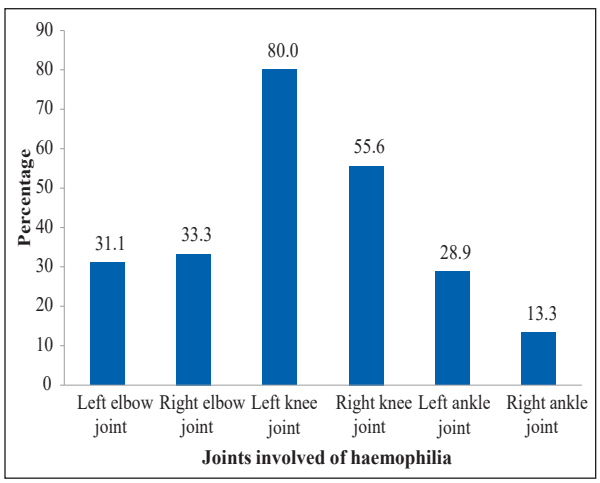

Figure 2. Bar diagram showing joints involved in haemophilia among the study patients (n=45).

Table I shows that more than half (51.1%) patients were found to score global gait score ≤1.

Table I: Distribution of the study patients according to global gait score (n=45)

Global gait score	Frequency	Percentage
≤1	23	51.1
2-3	22	48.9
Mean±SD	1.49	±0.66
Range (min-max)	0.0	-3.0

Table II shows that two third (66.7%) patients were found HJHS score 11-20. The mean HJHS score was found to be 15.8±4.4 with a range from 6.0 to 25.0.

Table II: Distribution of the study patients according to HJHS score (n=45)

HJHS score	Frequency	Percentage
≤10	8	17.8
11-20	30	66.7
>20	7	15.5
Mean±SD	15.8	±4.4
Range (min-max)	6.0	-25.0

In this study association between HJHS score and severity of haemophilia was not found to be statistically significant (p>0.05) (Table III and Figure 3), but there was positive significant correlation (r=0.536; p=0.001) between age and HJHS score (Figure 4).

Table III: Association between HJHS score and severity of haemophilia by factor levels (n=45)

	HJHS score						P value
	≤10 (n=8)		11-20 (n=30)		>20 (n=7)		
	n	%	n	%	n	%	
Mild (>5-40)	1	12.5	8	26.7	1	14.3	
Moderate (1-5)	6	75.0	14	46.7	2	28.6	0.261^{ns}
Severe (<1)	1	12.5	8	26.7	4	57.1	

ns= not significant. P value was calculated by chi square test.

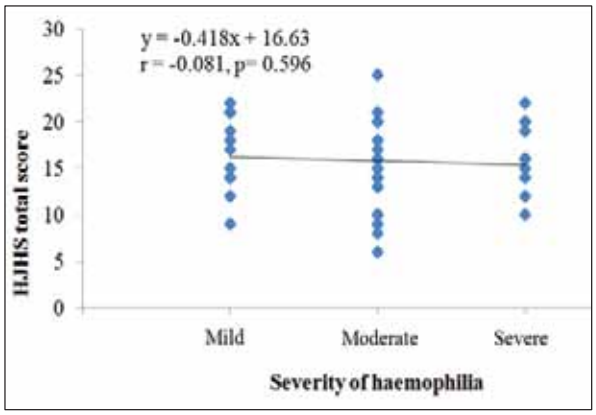

Figure 3. Scatter diagram showing no significant correlation (r= -0.081; p=0.596) between severity of haemophilia and HJHS score.

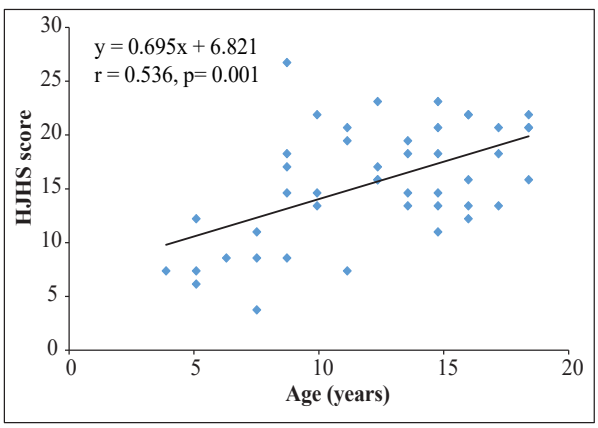

Figure 4. Scatter diagram showing positive significant correlation (r=0.536; p=0.001) between age and HJHS score.

Discussion

This is a descriptive cross-sectional study carried out to assess the relationship between HJHS and severity of haemophilia (factor levels), to estimate the condition of involved joint, to find out significant correlation between HJHS and age of the patients and to evaluate the joint status by global gait score. The present study findings were discussed and compared with previously published relevant studies.

In this study it was observed that 10 (22.2%) patients had mild haemophilia, 22 (48.9%) had moderate and 13 (28.9%) had severe haemophilia. In a similar study documented by Payal et al, the investigators found that 25 (44%) cases had severe disease, while 20 (36%) had moderate and 11 (20%) had mild.[3] Trakymiene et al consisted that in their study haemophilia was mild in 17%, moderate in 15% and severe in 68%.[7] Uddin et al have also found 18 (45%) cases had mild haemophilia, 17 (42.50%) had moderate haemophilia and five (12.50%) cases were diagnosed as severe haemophilia.[8] Karim et al reported that among haemophilia A, 52.5% were mild and 47.5% were moderate, on the other hand, 40% of haemophilia B presented with mild disease, 50% with moderate form and 10% with severe disease.[9] Zafar et al in a study reported clinical stratification as severe, moderate and mild haemophilia seen in 55.55%, 18.8% and 25.64% cases, respectively.[10] Borhany et al documented that majority of haemophilia had moderate severity (52.0%) both in haemophilia A and haemophilia B.[11] A study from Egypt showed that severe manifestations were reported in majority in 76.7% followed by moderate severity in 17.2%.[12]

In this study, it was observed that joint involvement was mostly found in left knee joint (36 patients, i.e., 80.0%), followed by right knee joint, right elbow joint, left elbow joint, left ankle joint and right ankle joint. In a study of Qasim et al the investigator found haemarthrosis was seen in 86% of the patients, 14% patients had no joint involvement.[13] 15.7% patients had single joint involvement and three to six joints were involved in 43.1% of patients. Knee joint was the most commonly involved joint (47.83% episodes), and among knee joints, right knee was more commonly involved (53% patients). Payal et al reported that knee joint was the predominant joint affected by haemarthrosis (67.85% cases).[3] Ankle joint was involved in 51.78% cases and elbow joint in 35.71% cases. Similar results were observed by Karim et al in

their study, knee joint swelling was present in 68% cases of haemophilia followed by ankle joint (22%), elbow joint (14%), shoulder joint (8%), and hip joint involvement (6%).[9] They also found knee joint swelling was present in 58% cases of haemophilia A and 10 % cases of haemophilia B. Ankle joint involvement was found in 36% cases of haemophilia A and 8% cases of haemophilia B, Elbow joint swelling was found in 12% of haemophilia A and 2% cases of haemophilia B. Shoulder joint and Hip joint involvement were found in 8% and 6% cases of haemophilia A only.In a study by Mohsin et al on haemophilia B patients, most commonly involved joint was found to be knee in 15 cases (33.3 %), followed by elbow in 17.7 %, ankle in 13.3 %, and hip joint in 4.5%.[14] Our result shows more involvement of knee joint with abnormal gait due to more physical activity.

This study shows more than half (51.1%) patients were found global gait score ≤1; with mean global gait score was 1.49±0.66 ranging from 0.0 to 3.0. Payal et al demonstrate the total joint scores and global gait score were then combined for a total score ranging from 0 to 124.[3]

In this study it was observed that two third (66.7%) patients were found to have HJHS score 11-20. The mean HJHS score was found 15.8±4.4 with a range from 6.0 to 25.0. Payal et al documented that maximum number of patients (40.47 %) had HJHS score of zero which means that there was no joint involvement.[3]

In this study association between HJHS score and severity of haemophilia was not found to be statistically significant. In the study conducted by Payal et al out of total 56 enrolled patients HJHS score was drawn in 42 patients. Out of 42 cases 21 (50%) had severe, 13 (31%) had moderate and 8 (19%) had mild haemophilia.[3] The mean HJHS score of severe, moderate, and mild haemophilia was 7.61±9.34, 5.69±9.96 and 6.37±7.38 respectively and difference was not statistically significant ($p>0.05$). Spearman correlation coefficient was 0.07 and p value was ($p = 0.64$) which is statistically insignificant. Their result was also similar with this present study. In another study, 17 patients had severe haemophilia A (residual factor activity ≤1%) and nine had moderate haemophilia A. The mean HJHS for moderate haemophilia was 4.83±5.27 and severe haemophilia was 8.27±6.11; $p=0.24$.[15] They found HJHS score not only depends on severity of haemophilia but also on other factors like age of patients, number of joint bleedings, age of first joint bleeding, physical activity limit, body mass index and presence of target joint.

In this study positive significant correlation ($r=0.536$; $p=0.001$) between age and HJHS score was observed. Similarly, Payal et al found HJHS score showing significant positive correlation with age of patient.[3] Spearman correlation coefficient was 0.54 and p value was ($p<0.0001$) which is statistically highly significant. So, with increasing age HJHS scores increase. Zeze et al observed that there were statistically significant positive correlations with a P-value of less than 0.05 between HJHS with age of patients.[16] Several studies have reported a positive relationship between age and HJHS values. For example, the Lithuanian study found higher joint scores in older children.[7]

The age & utility of the HJHS in assessing the health status of the joints was also tested on 20 Chinese children with haemophilia (age 5-17 years, haemophilia A/B: 18/2; severe/ moderate/unknown: 5/13/2). The HJHS score ranged from 1 to 35 (mean 13.1, median 12, SD 9.03). The investigators stated that the score was significantly higher in older children,but not specified exactly from which age the score noticed to be higher.[17] Similar results are reported by Trakymiene et al who reported that the mean total HJHS in the study cohort (n = 20) was

24.5, with a range from 5 to 50. The HJHS score ranged from 1 to 35 (mean 13.1, median 12, SD 9.03).[7] The investigators of that report stated that the score was significantly higher in older than in younger children, but it was not specified exactly from which age the score was noticed to be higher.[7]

Conclusion

Haemophilia is a debilitating and life-threatening disease that affects mostly knee, ankle and elbow joints. Significant correlation between the ages of patient with HJHS score was observed, but no significant correlation was found between HJHS score and severity of haemophilia. This study finding will help in future to assess the joint conditions and complications at early stage and will encourage to introduce prophylactic treatment approach instead of the on-demand treatment approach where feasible.

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