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Functional Independence Score in Haemophilia (Fish) for Children with Haemophilia: A Cross Sectional Study

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KEYWORDS
Functional Independence Score In Haemophilia (Fish), Haemophilia , Haemophilic arthropathy

ABSTRACT:

INTRODUCTION- Functional Independence Score in Haemophilia (FISH) is a performance-based assessment tool, to measure the patients' musculoskeletal functional ability. This study focuses on assessing the functional abilities of hemophiliac patients presenting to a tertiary care center.

MATERIAL METHODS- This hospital-based observational study was performed on 87 patients diagnosed with hemophilia. Patients between 4 to 18 years old were selected. Each patient was evaluated in seven activities under three categories: self-care (grooming and eating, bathing, and dressing), transfers (chair and squat), and locomotion (walking, running, and step climbing). Each activity was graded from 1 to 4 according to the amount of assistance required to perform the activity with total scores ranging from 7 to 28.

RESULTS- Patients in the majority belonged to the age group interval of 9-13 years, 11 months (36.8%) with a mean FISH of 29.44 in 4-8 year,11-month intervals with a maximum incidence of Haemophilia-A(91.95%). Mean FISH score was highest in cases of mild Haemophilia(31.66), and least in severe Haemophilia(24.05). Inhibitors and types of disease (Haemophilia-A and Haemophilia-B) were comparable with each other. Majority of cases belonged to score 4 in Eating and Grooming(81.6%), Dressing Score(43.7%), Chair Score(46%), Walking Score(60.9%), Stair score(40.2%), Running Score(31%). Squatting Score had the majority of cases in score 1(48.3%). Significant statistical difference was evident between severity and squatting, stair, and running scores (all p-values<0.001)

CONCLUSION- The functional components like squatting were affected depicting majorly knee joint involvement which was also statistically associated with severity.

1. INTRODUCTION-

Haemophilia, X-linked recessive disease is caused by genetic alterations that result in lower levels of factor-VIII and IX, affecting the cycle of haemostasis predisposing to profuse bleeding with or without trauma.[1,2] According to Annual Global Survey (AGS) 2019 world federation of haemophilia(WFH) in 115 countries, 195,263 total cases of haemophilia were identified. Out of these cases, 157,517 were suffering from Haemophilia-A, 31,997 from Haemophilia-B, and 5749 had unknown Haemophilia. The approximate

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incidence of haemophilia is 1:10000 live birth worldwide.[3] According to Indian report, incidence of haemophilia was around cases, of which 19,690 were Haemophiliac-A, 3150 were Haemophiliac-B and rest were unknown haemophiliacs.[3] Haemophilia-A is common as compared to haemophilia-B accounting 80%- 85% of total cases.[4] Clinical presentation can vary like neonates presenting with intracranial bleeding to children with internal bleeding, repetitive painful or inflamed joints leading to haemophilic arthropathies which increases with physical activity.[5] This consequences to contractures and functional disability even in 1st decades of life.[2] The treatment in haemophilia consist of intravenous replacement of the decreased levels of clotting factors. [6,7] Since, arthropathy seems irrevocable, tools used to detect the functional status of joint are important for assessing the degree of damage to joint for better outcomes. [6-8] Functional Independence Score In Haemophilia (FISH) is dependable, cost-effective and user friendly tool to evaluate joints status and is a performance based assessment tool.[9] It objectively measures the patients functional independence consisting of 8 basic routine activities. By identifying the risk factors influencing positive or negative impact on functional status of haemophilic children, helps decrease the morbidity and mortality.[9-10] Hence, present study intended to conduct a clinical evaluation and usefulness of FISH in children having haemophilia and correlate the findings.

2. MATERIAL AND METHODS-

This single centre, hospital based cross-sectional observational study was conducted in department of Paediatric at tertiary care hospital located in Central India. 87 patients were included in the study by convenience sampling Technique.[10] Patients ranging from 4 years to 18 years of age diagnosed with Haemophilia visiting the Out-Patient Department of Paediatric over a period of 2 years were included in the study. Patients with major systemic disease with co-morbidities which might confound the study findings were excluded from the study. After explaining the study procedure, written informed consent obtained from all the subjects selected for the study. Case records were collected from the medical records department after availing necessary ethical approval from the institution and were meticulously looked for various aspects such as name, age, detailed address, education, monthly income of parents were identified. Functional independence was assessed by taking history of the patient. Each patient was evaluated for seven activities under three categories: self-care (grooming and eating, bathing, and dressing), transfers (chair and floor), and mobility (walking and step climbing). Each activity was graded from 1 to 4 according to the amount of assistance required to perform the activity: 1 = the subject is unable to perform the activity or needs complete assistance to perform the activity; 2 = the subject needs partial assistance/aid/modified instruments/modified environment to perform the activity; 3 = the subject is able to perform the activity without aid or assistance, but with slight discomfort (the patient is unable to perform the activity like healthy peers); and 4 = the subject is able to perform the activity without any difficulty like other healthy peers. The total score ranged from 7 (the worst) to 28 (the best functionality). The patients were separated according to the severity of haemophilia (mild form with factor level >0.05 to 0.40 UI/ml, moderate form with factor level 0.01 to 0.05 UI/mL, and severe form with factor level <0.01 UI/mL). Eating and bathing were replicated in the outpatient clinic using acceptable alternatives, albeit they are best done in the child's home environment. The collected data were tabulated and statistically analyzed using SPSS© for windowsTM Vs 17, IBMTM Corp NY and Microsoft excelTM 2007, Microsoft® Inc USA. Kolmogorove- Smirnove analysis was performed for checking linearity of the data and Chi square test was used to analyze the significance of difference between frequency distribution of the data. P value <0.05 was considered as statistically significant.

3. RESULTS-

"Table I: Baseline characteristics of patients included in the study (n=87)"

		Frequency	Percentage
Age Group	4-8 year 11 month	27	31%
	9-13 year 11 month	32	36.8%
	14-18 years	28	32.2%
	Total	87	100%
Type of Disease	HAEMOPHILIA - A	80	91.95 %
	HAEMOPHILIA - B	7	8.05%
	Total	87	100%
Severity	MILD	3	3.4%
	MODERATE	14	16.1%
	SEVERE	70	80.5%
	Total	87	100%

Patients demographic data showed that children of age group 9-13 year and 11 months had the maximum

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frequency which is 36.8% and the minimum frequency was found in 4-8 year and 11 months' age which is 31%. Mean FISH score found in age interval of 4-8 year 11 month was the highest (29.44). Clinical type wise our study had majority of Haemophilia-A (91.95%) with mean FISH score 24.9 and only few were cases of Haemophilia-B (8.05%) with maximum severity type (80.5%) and mean FISH score of 26.

Table II: Distribution of children according to Severity according to parameters in FISH (n=87)"

		Frequency	Percentage
Eating, Grooming score	2	5	5.7%
	3	11	12.6%
	4	71	81.6%
	Total	**87**	**100%**
Bathing Score	2	5	5.7%
	3	20	23.0%
	4	62	71.3%
	Total	**87**	**100%**
Dressing Score	1	1	1.1%
	2	17	19.5%
	3	31	35.6%
	4	38	43.7%
	Total	**87**	**100%**
Chair Score	2	10	11.5%
	3	37	42.5%
	4	40	46.0%
	Total	**87**	**100%**
Squatting Score	1	42	48.3%
	2	22	25.3%
	3	10	11.5%
	4	13	14.9%
	Total	**87**	**100%**
Walking Score	1	1	1.1%
	2	2	2.3%
	3	31	35.6%
	4	53	60.9%
	Total	**87**	**100%**
Stair Score	1	7	8.0%
	2	22	25.3%
	3	23	26.4%
	4	35	40.2%
	Total	**87**	**100%**
Running Score	1	19	21.8%
	2	25	28.7%
	3	16	18.4%
	4	27	31.0%
	Total	**87**	**100%**

Mean FISH score was highest in cases of mild haemophilia (31.66), followed by cases of moderate haemophilia (28.57) and severe haemophilia (24.05). Inhibitor and types of disease (haemophilia-A and haemophilia-B) were comparable with each other with no statistical significant difference found (p-value= 0.545). Maximum cases were opting occasional physiotherapy sessions (63.2%) with mean FISH score of 23.43 and few were on regular basis physiotherapy sessions (36.8%) with mean FISH score of 27.81. We assessed our case's distribution based on their participation in these activities and found that according to Eating and Grooming Score majority of them belonged to score 4 (81.6%), and bathing score of 4 was found in majority (71.3%). Dressing Score evidently showed that majority of them belonged to score 4 (43.7%), chair Score showed that majority of them belonged to score 4 (46%), squatting Score had majority cases in score 1 (48.3%), majority walking Score to score 4 (60.9%) while majority stair score belonged to score 4 (40.2%).

Table III: Association of children between their Severity and parameters in FISH (n=87)

	EATING AND GROOMING			**P value**
	2	3	4	
MILD	0 (0%)	0(0%)	3(3.44%)	0.868
MODERATE	1(1.15%)	1(1.15%)	12(13.80%)	
SEVERE	4(4.60%)	10(11.5%)	56(64.36%)	
	BATHING			
	2	3	4	
MILD	0(0%)	0(0%)	3(3.44%)	0.646
MODERATE	0(0%)	3(3.44%)	11(12.65%)	
SEVERE	5(5.75%)	17(19.55%)	48(55.17%)	
	DRESSING			
	1	2	3	4	
MILD	0(0%)	0(0%)	0(0%)	3(3.44%)	0.571
MODERATE	0(0%)	2(2.30%)	5(5.75%)	7(8.04%)	

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SEVERE	1(1.15%)	15(17.25%)	26(29.89%)	28(32.18%)	
	CHAIR SCORE				
	2		3	4	
MILD	0(0%)		0(0%)	3(3.44%)	0.052
MODERATE	0(0%)		4(4.60%)	10(11.50%)	
SEVERE	10(11.50%)		33(37.93%)	27(31.03%)	
	SQUATTING				
	1	2	3	4	
MILD	0(0%)	0(0%)	1(1.15%)	2(2.30%)	0.001**
MODERATE	3(3.44%)	3(3.44%)	2(2.30%)	6(6.90%)	
SEVERE	39(44.83%)	19(21.84%)	7(8.05%)	5(5.75%)	
	WALKING				
	1	2	3	4	
MILD	0(0%)	0(0%)	0(0%)	3(3.44%)	0.131
MODERATE	0(0%)	0(0%)	1(1.15%)	13(14.95%)	
SEVERE	1(1.15%)	2(2.30%)	30(34.49%)	37(42.52%)	
	STAIR SCORE				
	1	2	3	4	
MILD	0(0%)	0(0%)	0(0%)	3(3.44%)	0.012*
MODERATE	0(0%)	1(1.15%)	2(2.30%)	11(12.64%)	
SEVERE	7(8.05%)	21(24.14%)	21(24.14%)	21(24.14%)	
	RUNNING				
	1	2	3	4	
MILD	0(0%)	0(0%)	0(0%)	3(3.44%)	0.004**
MODERATE	0(0%)	2(2.30%)	3(3.44%)	9(10.34%)	
SEVERE	19(21.84%)	23(26.44%)	13(14.95%)	15(17.25%)	

Running Score showed that majority of them belonged to score 4 (31%). In evaluating association between severity grades and elements of FISH score, we could not find statistical significant difference between Severity and elements like Eating Grooming Score, bathing Score, and weight bearing activities like chair, walking Score (p-value =0.868, p-value =0.646, p-value =0.052, p-value =0.131 respectively). We could establish significant statistical difference between severity and squatting, stair and running scores (all p-values <0.001).

Table IV: FISH Score mean according to different parameters(n=87)

PARAMETERS		**FISH SCORE(MEAN)**
PHYSIOTHERAPY	Occasional	23.43
	Regular	27.81
TYPE OF DISEASE	Haemophilia – A	24.96%
	Haemophilia – B	26%
AGE	4-8 year 11 month	29.44
	9-13 year 11 month	24.62
	14-18 years	21.28
SEVERITY	Mild	31.66
	Moderate	28.57
	Severe	24.05

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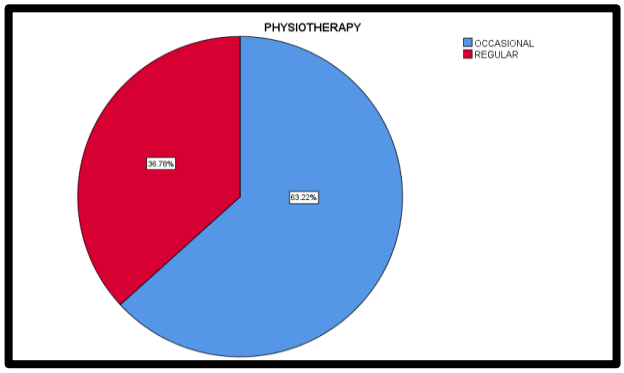
Figure I: Distribution of children according to physiotherapy (n = 87)



4. DISCUSSION-

Haemophilia is an X-linked inborn and innate bleeding disorder which is a recessive mutation. This leads to a decrease in levels of clotting factor VIII or factor IX. Literature has evidenced mutations over hundreds and thousands in the genes which encode for factor VIII and IX. Moreover, literature has also enlightened about 30% spontaneous mutation leading to this disease.[11] X-linked recessive pattern are inherited in both haemophilia A and B cases with all of female child born from haemophilia fathers will be carriers, and no males will be born affected with haemophilia. presenting symptom which is very common is excessive bleeding into joints, most commonly affected joint is knee.[2] Children presents with frequent and unremitting intra-articular and intramuscular bleeding episodes. This sequels into joint and soft tissue damage, therefore, persuading to arthropathy and musculoskeletal dysfunction.[12]

1) Baseline characteristics-

In our study, maximum cases prevailed in age group interval of 9-13 year and 11 months (36.8%). Haemophilia-A (91.95%) with mean FISH score 24.9 was most common type we appraised in our study. Haemophilia-B (8.05%) contributed to 80.5% cases with mean FISH score of 26. Maximum cases were opting occasional physiotherapy sessions (63.2%) and few were on regular basis physiotherapy sessions (36.8%). Our study findings were in consensus with study conducted by Tlacuilo-Parra et al**.** where they found delineated mean age of 10.93.4 (range 5–16 years old).[10] On the contrary, Ferreira et al., found that mean age 36.8 +16.8 years ranging from 18 to 79 years, these findings were opposite to our results.[2] Also, in study of Ghany et al, they reported mean age was 10.6 ± 2.95 years ranging from 6 to 16 years.[13] Shamoon et al also noticed that **t**wo-third cases were below 10 and only two children aged >40 years prevailed.[14] Pollmann et al. disclosed that, 50% children had severe haemophilia, the early haemarthrosis occurs during the first year of life.[15] Malathi et al., showed 48% of children were on regular physiotherapy but that did no significantly improve their FISH score. The author said that the investigators found that the children were doing exercise with intention to reduce the effect of impairment and not for purpose of strengthening their joints. More studies are required to throw a light into what type of exercise the children are actually undergoing.[16]

2) Distribution of children according to score—

FISH assesses a children's functional independence in executing eight activities divided into three categories: self-care (grooming and eating, bathing, and dressing), transfers (chair, squatting), and mobility (walking, running and stair climbing).[10] We assessed our children's distribution based on their participation in these activities. It determines if the children is capable of performing activities such as self-care, transfers, and mobility on his or her own. It possesses strong internal consistency, indicating that all elements of the instrument played a significant role in the final score.[9] Distribution of children according to Eating and Grooming Score revealed that majority of them belonged to score 4 (81.6%) followed by score of 3 (12.6%) and score of 2 (5.7%), which indicate that majority children with haemophilia were functionally independent for eating and grooming. This scores convey that involment of upper limb joints like elbow and shoulder was very minimal in our subjects. Distribution of children according to Bathing Score showed that majority of them got score of 4 (71.3%) followed by score of 3 (23%) and score of 2 (5.7%). Maximum children from our study were not or less dependent for bathing function with optimal functioning of elbow and shoulder joints. Dressing Score evidently showed that majority of them belonged to score 4 (43.7%) followed by score of 3 (35.6%), score of 2 (19.5%) and score of 1 (1.1%), indicating that majority of children were functionally independent in using their shoulder and elbow joints for self care and grooming. Chair Score showed that majority of them belonged to score 4 (46%) followed by score of 3 (42.5%), and score of 2 (11.5%). This conveyed that activity of chair transfer carried highest number of cases who did not need any external aid for performing it, implying no involvement of hip joint. Squatting Score revealed that majority of them belonged to score 1 (48.3%) followed by score of 2 (25.3%), score of 4 (14.9%) and score of 3 (11.5%). This coneys that,

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majority of our cases had knee joint involvvement, making them unable to squat without assistance. Squatting is an important activity that Asian and African people engage in on a regular basis. For e.g. Squatting in the toilet, this varies slightly in western countries, as adults in those countries squat for gardening. Furthermore, children or youngsters squat when engaging in tasks such as putting on shoes. In reality, a high-flex knee prosthesis was developed for the current generation since the knee joint required more range of motion. Therefore, it can be concluded that squatting posture may not be a frequently needed functional activity globally. Although it is a part of instrument, and could be of particular use in those with perceptibly less knee joint damage. Walking Score proved that majority of them belonged to score 4 (60.9%) followed by score of 3 (35.6%), score of 2 (2.3%) and score of 1 (1.1%) having functional independency for mobility with normal gait and optimal hip joint. Stairs Score moreover enlightened that majority of them belonged to score 4 (40.2%) followed by score of 3 (26.4%), score of 2 (25.3%) and score of 1 (8%). Stair case climbing is a task that demands an optimal weight bearing activity capacity by hip joints. In our study, maximum cases had functional hip join with no involvement in damage. Running Score showed that majority of them belonged to score 4 (31%) followed by score of 2 (28.7%), score of 1 (21.8%) and score of 3 (18.4%), indicating a haelthy hip and ankle joint status for mobility in terms of running with functional independency. Step climbing, squatting and walking obtained lower scores than other physical activities (2.84 ± 0.79, 2.92 ± 0.88 and 3.18 ± 0.77 respectively) by Hassan et al.[17] Malathi et al., found that lowest mean score was for weight bearing activities like squatting (2.71±1.25), mobility like running (2.60±1.3) and then weight bearing like stair climbing (2.97±1.1), while running (2.60±1.3) had the least mean score.[16] Tlacuilo-Parra et al. witnessed 39 children (65%) were rated as functionally totally independent in all seven activities without the need of any external aid, 14 children (23%) performed the activity efficiently with slight discomfort and without asking for external help, and 7 children (12%) needed partial assistance to carry out the activity. The tasks that scored least were squatting, walking, and step climbing, being step climbing the most drastically affected activity. These study findings were in accordance with our study results.[10] Padankatti et al., found that most children had difficulty in undergoing the tasks in all eight domains of FISH. Sixteen children (24%) faced difficulties in self-care activity like eating and grooming, and 66–93% of the children had problems in rest domains. It was found that 62 children (93%) needed assistance in mobility like running and Walking (79%) as well. The most significant abnormality noted was in the weight bearing activity of chair transfer.[18]

3) Association of children between severity and scores-

The therapist can later decide whether to initiate therapy by treating the functional inability, or put the children on alternate modifications enabling them to perform the activity efficiently. This aids the children's functional independence comprehensively. Therefore, we tried to evaluate association between severity grades and elements of FISH score. We found significant statistical difference between severity and FISH elements like squatting, stair and running scores (all p-values <0.001). No association was evident amongst rest of the FISH elements. Our study findings were supported by Tlacuilo-Parra et al. They found that, comparing mild to moderate group, four activities namely chair transfers (3.81 ± 0.39; p-value =0.042), squatting (3.63 ± 0.49; p-value=0.002), walking (3.59 ± 0.59; p-value=0.003), and step climbing (3.54 ± 0.59; p-value=0.001) had strong statistical difference. On the other hand, compared to the severe haemophilia group, the moderate group had only two activities with significant difference: bathing (3.47 ± 0.73; p-value =0.030) and dressing (3.47 ± 0.73; p-value=0.030).[10] Ferreira et al. could not inveterate statistical difference between children with severe grade and moderate grade haemophilia in relation to mean functional independence score (16.37 vs. 15.66; p-value = 0.827), yet the evaluation results for children with mild haemophilia were significantly higher (32.25 vs. 16.84; p-value = 0.001).[2]

4) Association of children between their inhibitor and types of disease-

In current study, we focused on association of children between their inhibitor and types of disease. We found that Inhibitor and types of disease (haemophilia-A and haemophilia-B) were comparable with each other with no statistical significant difference found (p-value= 0.545) Kachooei et al. found that the children managed with inhibitors had lesser level of function. Inhibitor forms in range of 1 of 4 children with severe grade of haemophilia A after the transfusion of first factor VIII. Inhibitor forms in 1 of 50 children with mild or moderate grade haemophilia A destroyed the children's own factor VIII as well as transfused factor VIII and worsened the case to severe haemophilia.[19]

5. CONCLUSION-

We have documented the widespread prevalence of haemophilic arthropathy, which is a preventable disability. The assessment of joint health is one of the most important goals in haemophilia care. FISH

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assessment is easy to use and applicable as a performance-based assessment tool particularly for countries with limited availability of coagulation factor concentrates, where early, more severe arthropathy is expected. FISH appears to be a promising disease-specific instrument for assessing overall musculoskeletal function in haemophilia. It requires evaluation in different patient populations.

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8. CONFLICT OF INTEREST- The authors declare that they need no conflict of interest.

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