Clinical Profile of Adult Hemophilia Patients with Special Reference to FISH and WFHPE Score: An Observational Cross-sectional Study

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ABSTRACT
Background and objectives: Hemophilia is an X-linked recessive inherited disease affecting the coagulation pathway due to congenital deficiencies in either factor VIII (hemophilia A) or factor IX (hemophilia B). The clinical assessment of a patient’s functional ability and the state of joint conditions is carried out by the clinicians by administering questionnaires namely the Gilbert or the World Federation of Hemophilia Physical Examination (WFH-PE) score for joint condition and Functional Independence Score in Hemophilia (FISH) for joint function.

Here, we have studied the clinical profile of adult hemophilia patients with the short- and long-term complications of the disease. Additionally, the FISH score and the Gilbert score are calculated to assess functional independence and joint condition, respectively. The scores were also compared according to the severity of the disease.

Materials and methods: An observational cross-sectional study of 40 adult hemophilia patients was carried out in Sir Sayajirao General Hospital and Medical College, Baroda, Gujarat, India, over a period of 1 year. Data regarding age, sex, and complications associated with the disease were collected in the form of a questionnaire. The overall mean and standard deviation (SD) of FISH and Gilbert scores were calculated and correlated with the severity of the disease.

Results: The majority of cases (19) were between 20 and 40 years, and most (24) were diagnosed in childhood. All the subjects were male and all except one had hemophilia A. Family history was seen in only half of the cases. Nine had mild, 20 had moderate, and 11 had severe disease. Among 46% of the subjects had joint arthropathy with the knee joint most affected (60%) followed by the ankle (22.5%). The mean FISH score was 27.132 ± 4.0691 with a minimum score of 15 in severe disease suggesting more functional deficit. The average Gilbert score was 7.4 ± 2.985 with a maximum score of 14 in severe disease suggesting more joint damage.

Interpretations and conclusion: All subjects were male and except one all had hemophilia A. Majority were between 20 and 40 years but most were diagnosed before 10 years of age and only 50% had positive family history. Arthropathy is the most common complication with the knee joint being most affected. Majority of mild hemophiliacs achieved a maximum FISH score denoting maximum functional capacity. Compared to existing studies, our study showed better FISH scores in moderate hemophiliacs suggesting more functional independence. While comparing Gilbert’s score to other studies, moderate and severe hemophiliacs in our study showed less joint damage.

INTRODUCTION
Hemophilia is a hereditary disorder of the coagulation pathway. Both hemophilia A and B (which are the two main types) are single-gene disorders consisting of mutation in gene encoding factors VIII and IX, respectively, causing deficiency of these factors. Globally, one in 1,000 people manifest with bleeding disorders out of which hemophilia A constitutes 70% of cases.¹

In India, the prevalence of hemophilia A is about 0.7 per 1 lakh population. Similarly, the prevalence of hemophilia B is 0.1 per 1 lakh in India; compared to 1.3 per 1 lakh in the United States (US) (13 times lower in India).¹ However, the US has a more robust surveillance system, whereas, in India, the underdiagnoses of cases is prevalent.¹

Male subjects show clinical symptoms, while females carrying the mutated gene are asymptomatic because of the X-linked recessive pattern of inheritance of the disease.² A male receives his only X chromosome from his mother; hence he has a 50% chance of inheriting the disease from a healthy mother, unlike a female who would have to inherit two defective alleles from both her parents. However, 30% of cases have no family history and 80% of those women are carriers of de novo mutated allele.

Due to the deficiency of clotting factors VIII and IX involved in the intrinsic and common coagulation cascades, the risk of hemorrhage or thrombosis is increased in disorders like hemophilia. The disease is clinically categorized into mild, moderate, and severe based on the deficient factor activity. Severe bleeding is commonly noticed at the sites such as joints (knee joints are most common), mucus membranes and gums, and genitourinary tract, with cases like intracranial, gastrointestinal tract (GIT), and neck bleeds posing a significant threat to life.

Bleeding from joints is a major problem, which is often recurrent and chronic, leading to extensive articular cartilage destruction, synovial hyperplasia, joint deformity, muscle atrophy, and contracture formation. Overtime, these lead to joint deformities, physical dependence, and functional disability. Therefore, the onus is on the treating physician to prevent this functional disability and hence more light has to be shed on factors leading to joint deformity.

The World Federation of Hemophilia Physical Examination (WFH-PE) (Gilbert) score measures the health of joints affected by bleeding by scoring the degree of pain, and bleeding, and performing a physical examination of the joint.³ To assess the functional ability of the joint objectively, however, another easily administrable scale called Functional Independence Score in Hemophilia (FISH) is used. Patients are evaluated for seven activities under three categories: self-care, transfers, and mobility.⁴

Here, we aimed to study the clinical profile, severity of disease, common sites of bleeding, and complications in 40 hemophilia patients along with evaluation of structural joint damage using the WFH-PE score and functional deficits using the FISH score.

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Materials and Methods

After obtaining approval and clearance from the Scientific Review Committee and Institutional Ethics Committee for human research, a population-based, observational cross-sectional study of 40 hemophilia patients was undertaken at a tertiary care hospital in Vadodara, Gujarat, India over a period of 1 year (2018–2019).

All hemophilia A and B patients over 12 years of age who were admitted into various wards, follow-up clinics, as well as those who came for replacement therapy, were included in the study. Some cases were enrolled from the Haemophilia Society Chapter One registry.

After getting written consent from patients, data was collected in the form of a questionnaire. Data were collected regarding sociodemographic characteristics, presenting complaints, age at diagnosis, clinical presentation, type of hemophilia, and past history. Patients were examined for the site of bleeding, severity, and deformity. The clinical severity of the disease (mild, moderate, and severe) was decided by the deficient factor activity (normal: 50–100%, mild: 5–40%, moderate: 1–5%, severe: <1%).

The WFH-PE (Gilbert) score was calculated for each patient which measures the health of joints most commonly affected by bleeding (knees, elbows, and ankles), by scoring the degree of pain (0–3), bleeding (0–3), and performing a physical examination of the joint (0–12) (Table 1). A score of zero denotes normal joints; 68 points correspond to the worst level of arthropathy.5

However, another scale called FISH was used to assess the functional ability of the joint. Patients were evaluated for seven activities under three categories (self-care, transfers, and mobility), and were marked between 4 and 1 in decreasing order of ability (Table 2).

Score 4: Able to perform the activity without any difficulty.

Score 3: Able to perform the activity without aids or assistance, but with slight discomfort.

Score 2: Needs partial assistance/aids/modified instruments/modified environment to perform the activity.

Score 1: Unable to perform the activity or needs complete assistance to perform the activity.

Scores range from 8 to 32, with 32 being the highest level of independence.7

The mean value with standard deviation (SD) was calculated for both scores and compared with the severity of the disease.

Results

Out of a total of 40 patients, 19 patients (48%) were between 20 and 40 years of age, whereas the least number of patients were above 60 years of age (n = 4, 10%) (Fig. 1). However, most of the patients (n = 24, 60%) were diagnosed before 10 years of age. The pediatric population (age <12 years) was excluded from our study.

All the patients were male. Female hemophiliacs were not identified in the study population. Almost all (n = 39, 97.5%) except one patient had hemophilia A. Although being an inherited disorder, family history has been observed in only half of the cases among the study population.

While categorizing according to severity, 22.5% of cases (n = 9) belong to mild hemophilia in the study population, about half (50%) belong to moderate (n = 20), and 27.5% (n = 11) belong to severe hemophilia.

As can be seen in Figure 2, the knee joint was the most common site of bleeding (60%), followed by the ankle joint (22.5%).

Almost half of the patients in our study had arthropathy as the most common complication (46%), followed by gastrointestinal bleeding (25%) which was further divided into gum bleeding (n = 8, 20%), hematemesis (n = 1, 2.5%), and bleeding per rectum (n = 1, 2.5%) (Fig. 3).

When the FISH score was calculated for objectively evaluating functional ability and

![Fig. 1: Patient proportion according to age-groups](image)

![Fig. 2: Most common site of bleeding](image)
Clinical Profile of Adult Hemophilia Patients

In our study, patients with mild and moderate disease had a minimum FISH score of 24 and 25, respectively, whereas severe hemophiliacs had a minimum FISH score of 15. This finding suggests less functional independence. In the study conducted by Ferreira et al., the minimum FISH score in mild disease was 30, while scores of 16 and 14 were noted in moderate and severe disease, respectively.3 Compared to Ferreira et al’s study, in our study, patients with moderate disease had better FISH scores suggesting more functional independence.

The WFH-PE scale was developed in the 1980s to evaluate hemophilic arthropathy and is still widely used as it is easy to perform and capable of providing an extensive musculoskeletal assessment. The study conducted by Ferreira et al. showed a maximum Gilbert score of 6 in mild disease, 29 in moderate disease, and 34 in severe disease.3 However, our study reported a mean Gilbert score of 7.4 ± 2.985 and a maximum score of 10 in mild disease, 14 in moderate disease, and 14 in severe disease. As a maximum score suggests more joint damage, it can be said that patients with moderate to severe disease in our study suffered less joint damage compared to the study by Ferreira et al.3

**Limitations**

- The sample size was small and taken predominantly from a single center. Therefore, generalization of the result to a larger population would not be appropriate.
- Due to the small sample size, we were not able to establish a statistically significant correlation between the severity of disease with FISH and Gilbert scores, for which larger studies are required.

**Conclusion**

Out of a total of 40 patients, almost all the patients had hemophilic A except one with hemophilia B, suggesting a higher prevalence of hemophilia A compared to the studies conducted by Mishra et al., involving knee joint in nearly 57.1% of the patients.8

**Functional Independence Score**

In Hemophilia is a reliable, inexpensive, performance-based assessment tool to objectively measure the patient’s functional ability that can be easily administered by a trained nurse, doctor, or therapist, therefore, constituting a good alternative to evaluate joint status. In our study, three (7.5%) patients with hemophilia had functional independence (FISH) scores of <25. The mean FISH score in our study was 27.132 ± 4.0691 which was comparable to another study by Choudhary et al. with a mean FISH score of 28.10

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**Conclusion**

Out of a total of 40 patients, almost all the patients had hemophilic A except one with hemophilia B, suggesting a higher prevalence...
of hemophiliac A. All patients were male in our study. Almost half of our study population was between 20 and 40 years of age. However, most of them were diagnosed below 10 years of age. Family history was present in half of the cases. Bleeding into joints was the most common presenting complaint followed by gum bleeding. Half of the study population had a moderate form of the disease. Recurrent bleeding into the joint progresses to chronic progressive hemophilic arthropathy, and the knee joint was involved the most among all weight-bearing joints.

The FISH and Gilbert scores are extremely useful instruments in clinical practice in the absence of imaging studies such as magnetic resonance imaging, which are considered very sensitive to detect early joint damage but are costly and relatively inaccessible. Only 7.5% of patients had a low FISH score (<25), whereas the majority of mild hemophiliacs achieved a maximum FISH score. Severe hemophiliacs had a maximum Gilbert score (14) compared to mild hemophiliacs, suggesting more joint damage.

In our study, we have studied several parameters such as age, gender, type of hemophilia, presence of family history, the severity of disease, site of bleeding, common complications, and assessment of functional independence and joint damage by FISH and Gilbert score respectively, along with its relation to severity. Therefore, this study outlines detailed clinical, treatment, and functional profiles of hemophilia patients in a single study group.

REFERENCES