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Clinico-epidemiological profile of hemophilia patients in north India: An observational study

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Abstract:
Objective: *To describe the clinical and epidemiological profile of hemophiliac patients in north India.*
Materials and Methods: *This was an observational cross-sectional study. Patients of all age groups with hemophilia registered under department of Medicine were included. A detailed clinical history was elicited from the accompanying parent/guardian. Patients were further classified into mild, moderate, severe depending on lab records and factor VIII and IX assay levels.*
Results: *Out of the total 115 hemophilia patients, 108 patients were of hemophilia A and 7 of hemophilia B. 54.78% (63/115) were >18 years of age. Mean age of patients was 26.15 years. Majority of the patients had severe hemophilia i.e. 66% (76/115), 20.86% (24/115) had moderate disease while 13% (15/115) had mild form of the disease. Knee joint was observed to be as the target joint among 31.81% of the patients. In patients with severe form of hemophilia A, 49 out of 71 required regular replacement of factor VIII making it about 69% and 5 out of 7 required regular replacement of factor IX making it 57.14%.*
Conclusion: *The severe type of haemophilia type A was more common than mild and moderate types. The study also emphasizes the need to identify hemophilia as a disease of national concern and to initiate a national programme for diagnosis, prevention, care and support for hemophilia.*

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I. Introduction

Hemophilia typically refers to an inherited bleeding disorder caused by deficiency of coagulation factor VIII (hemophilia A), factor IX (hemophilia B). ●Hemophilia A – Inherited deficiency of factor VIII (factor 8); an X-linked recessive disorder. ●Hemophilia B – Inherited deficiency of factor IX (factor 9); also called Christmas disease; an X-linked recessive disorder.(1) Hemophilia is exclusively a disease of males with females being the carriers.(2) Hemophilia A is more common than hemophilia B. Hemophilia A is also more likely to be severe. Hemophilia A occurs in approximately 1 in 5000 live male births. Approximately two-thirds have severe disease. Hemophilia B occurs in approximately 1 in 30,000 live male births. Approximately half have severe disease.(3) Hemophilia is characterized as mild, moderate, or severe, based on the residual or baseline factor activity level expressed as a percent of normal or in international units (IU)/ML.(4) Factor levels typically correlate with the degree of bleeding symptoms. •Severe hemophilia – defined as <1 percent factor activity, which corresponds to <0.01 IU/mL. •Moderate hemophilia – defined as a factor activity level ≥1 percent of normal and ≤5 percent of normal, corresponding to ≥0.01 and ≤0.05 IU/mL. •Mild hemophilia – defined as a factor activity level >5 percent of normal and <40 percent of normal (≥0.05 and <0.40 IU/mL).(5) Clinical manifestations of hemophilia relate to bleeding from impaired hemostasis, sequelae from bleeding, or complications of coagulation factor infusion.Patients with more severe hemophilia are more likely to have spontaneous bleeding, severe bleeding, and an earlier age of first bleeding episode, which can begin as early as birth.(6) Common sites of bleeding in newborns include the central nervous system, extracranial sites such as cephalohematoma, and sites of medical interventions including circumcision, heel sticks, and venipunctures.(7) Bruising, joint bleeds, and other sites of musculoskeletal bleeding become more common once children begin walking. Common sites of bleeding in older children and adults include joints and muscles.(8) The overall frequency of bleeding has declined with greater use of prophylactic factor administration.It is estimated that 10–80% of people with hemophilia are present in developing countries such as India.(9) However, majority of them remain under-diagnosed or not registered. Given that the incidence of hemophilia A is one in 5,000 and hemophilia B is one in 30, 000, as in the US, one expects India to have close to 100,000 cases of hemophilia.

However, according to the World Federation of Hemophilia, with data provided by the Hemophilia Federation of India (HFI), only 13,448 patients are registered.[10] The clinical profile of hemophilia patients is rarely reported in India. Only hospital-based studies have estimated the burden of hemophilia because the epidemiological methods are not cost-effective for the measurement of rare diseases. Thus, registries remain the best source for obtaining the epidemiological data on these conditions.[11] Although the genetic basis of this disorder has been well studied in India, data regarding the number of patients, disease trends, demographic profile, costs incurred through a public health program have not been reported.[12] The objective of this study was to describe the clinical and epidemiological profile of hemophiliac patients in north India particularly in Punjab.

Aims and Objectives: To describe the clinical and epidemiological profile of hemophiliac patients in northern India.

II. Material and Methods

Study Design: An observational cross-sectional study was conducted in the department of Medicine of government medical college and Rajindra hospital, Patiala, Punjab, India. The study was during 2018 and approved by the ethical committee of the institute. The consent was taken from each participant's parent/guardian before enrolling in the study. The objective of the study was explained to the parent/guardian and confidentiality of identity was assured.

Study Participants: A total of 115 patients of all age groups with hemophilia registered under the hemophilia registry maintained by the department of medicine were included in the study. Out of the total 115 hemophilia patients, 108 patients were of hemophilia A and 7 of hemophilia B. The patients having factor deficiency other than factor VIII/IX were excluded from the study.

Methods: A detailed clinical history was elicited from the accompanying parent/guardian with special emphasis on the following parameters: Demographic features, duration of symptoms, symptom profile, family history, and number of previous transfusions. Detailed physical examination with special reference to the joints examination was done. The case was defined as physician-diagnosed patient of hemophilia A or B, who was further verified from records of laboratory diagnosis, and registration records. Depending on factor assay levels, mild, moderate, and severe hemophilia were defined as those having factor level of >5-30%, 1-5%, and <1% of normal activity, respectively.

III. Observation

This cross sectional study was carried out to study the demographic and clinical profile of patients of Hemophilia A and B from north India as registered in Government Medical College and Rajindra Hospital, Patiala. We have drawn the following results from this study:-

Table no 1: Age-wise distribution of registered Hemophilia patients

Age(yrs)	No. of cases of Hemophilia A	Percentage	No. of cases of Hemophilia B	Percentage
<1YR	2	1.85%	—	—
2-10	16	14.81%	3	42.85
11-20	29	26.85%	2	28.57
21-30	24	22.22%	1	14.28
31-40	23	21.29%	—	—
41-50	7	6.48%	1	14.28
>50	7	6.48%	—	—
TOTAL	108	100%	7	100%

Table 1 shows a total of 115 patients of Hemophilia have been registered with us at Rajindra hospital, Patiala in 2018. Of them, 2 patients were under 1 year of age, maximum number (31) of patients were between 11 to 20 years of age group. Total number of patients <18 years of age were 52 (45.21%) and >18 years were 63 (54.78%). Mean age of patients being 26.15 years.

Table No 2: District wise distribution of patients

District	Cases	%age
Fazilka	1	0.925
Barnala	1	0.925
Bathinda	2	1.85
Fatehgarh Sahib	9	7.82
Gurdaspur	1	0.925
Ludhiana	16	13.91

Mansa	9	8.33
Mohali	11	10.18
Nawasheher	4	3.7
Patiala	42	36.5
Ropar	4	3.7
Sangrur	15	13.0
Total	108	100

Table 2 shows the district wise distribution of patients of Hemophilia registered. Maximum number of registered patients (42) were from district Patiala followed by 16 patients from district Ludhiana, 15 from Sangrur and 11 from Mohali. Fazilka and Barnala reported 1 patient each.

Figure 1: Severity wise distribution of Hemophilia A patients depending on factor VIII levels.

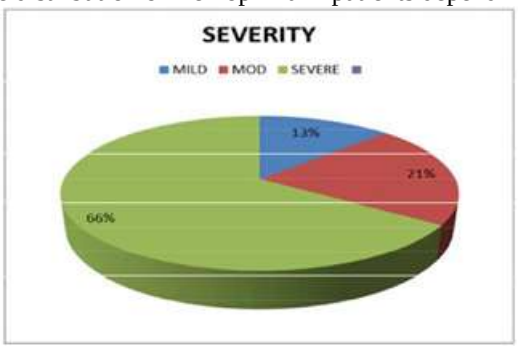


Figure 2 : Severity wise distribution of Hemophilia B patients depending on factor IX levels.

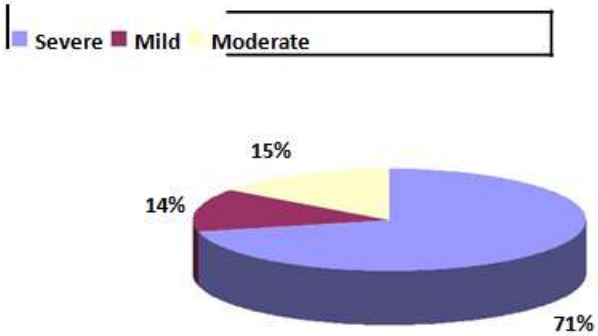
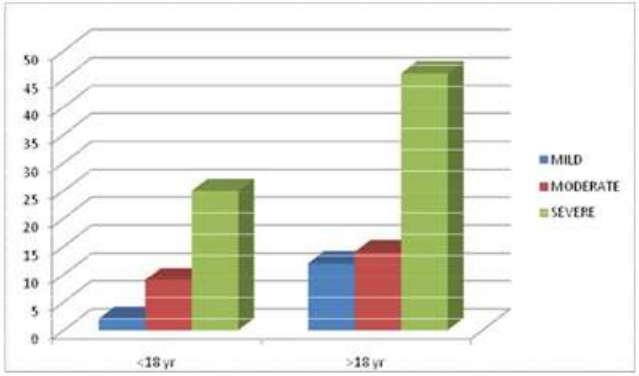


Figure 1 and 2 represents the severity wise distribution of patients. Of the total 115 patients, 71 patients (65.7%) had factor VIII levels of less than 1% and categorized as severe Hemophilia A. Moderate Hemophilia A with factor VIII levels between 1 to 5% were 23 cases (21.29%) while patients with factor VIII levels above 5% or mild form were 14 (12.96%). 5(71.42%) patients had factor IX levels less than 1% and categorized as severe Hemophilia B. Hemophilia B with factor IX levels between 1-5% and more than 5% were 1 case each.

Age-wise distribution shows 25 out of 36 (69.4%) patients below 18 years of age with severe hemophilia and 46 out of 72 (63.8%) above 18 years of age with severe form of the disease.

Figure 3: Age wise distribution of severity of disease



Out of the 115 patients registered, about 42 patients (38.8%) had no complaints related to the disease. 66 patients (61.11%) presented with manifestations such as bleeding from soft tissues or joints, swelling or pain the joints etc. As depicted in figure 5, knee is most common site of repetitive bleeding and hemarthrosis is most common presenting symptom. Hemarthrosis was commonest complication affecting the patients. Most common involved joint was knee joint (31.8%) followed by ankle (27.27%). 13 patients (12.03%) had involvement of more than one joints while 4 patients (6.06%) presented with bleeding from gums.

Figure 4: Frequency of bleeding manifestations and joint involvement in patients

Figure – 5: Factor VIII requirement in Hemophilia A.

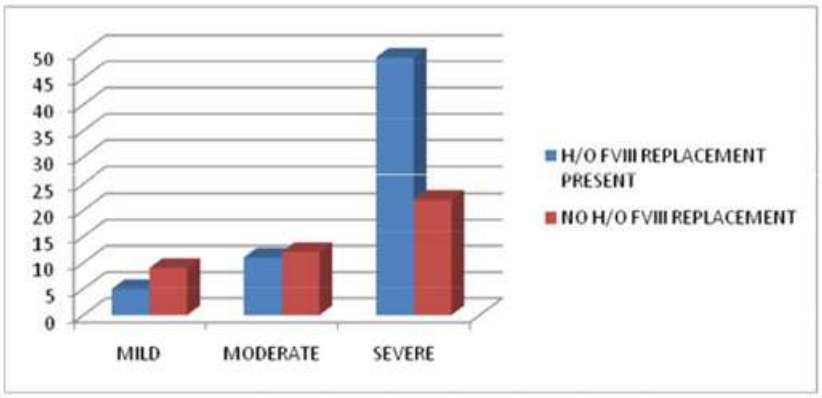


Figure 5 shows the presence of history of factor VIII requirement anytime during the course of illness. Patients with mild form of Hemophilia A, only 5 out of 14 had a history of factor VIII replacement post registration (35.7%) while those with moderate disease had 12 out of 23 cases (52.17%) with history of FVIII replacement. In patients with severe form of Hemophilia A, 49 out of 71 required regular replacement of factor VIII making it about 69%.

Figure – 6: Factor IX requirement in Hemophilia B

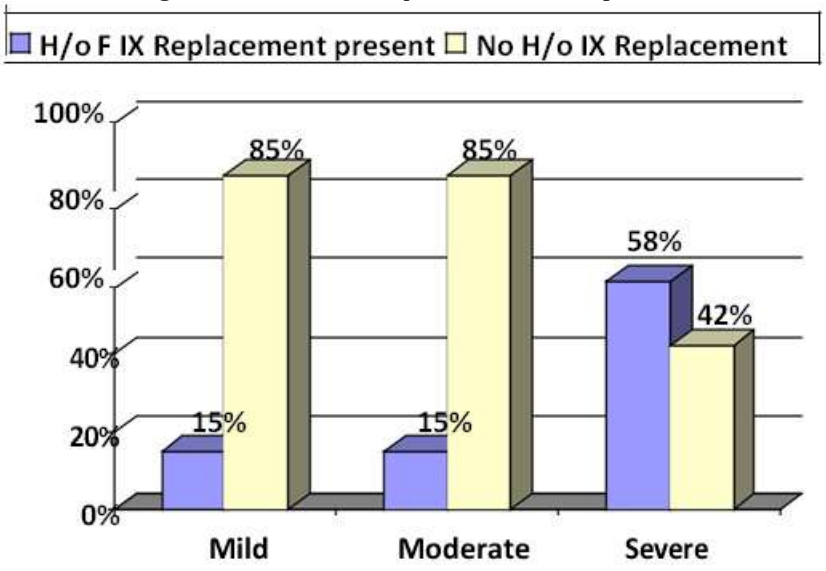


Figure 6 shows the presence of history of factor IX requirement anytime during the course of illness. Patients with mild form of Hemophilia B, only 1 out of 7 had a history of factor IX replacement post registration (14.28%) and those with moderate disease had 1 out of 7 cases (14.28%) with history of FIX replacement. In patients with severe form of Hemophilia B, 4 out of 7 required regular replacement of factor IX making it about 57.14%.

IV. Discussion

In this study, most of the patients had severe form of hemophilia A (65.7%) with 69.4% patients under 18 years and 63.8% patients above the age of 18 years having factor VIII levels less than 1%. Moderate hemophilia comes out to be 21.29% and mild deficiency amounts to 12.96%. This is similar to the findings reported by Parthiban et al[(13)] in which hemophilia A showed 66% of cases with severe factor deficiency, 26% with moderate, and 8% with mild deficiency. Our findings of severity of hemophilia are similar to those of Agarwal et al[(14)] Hazewinke et al[(15)] in South Africa and Kim et al[(16)] in their study on Korean population also showed similar results with percentage of severe hemophilia (55.7%). In study by Mishra el al[(17)] 66.2% (51/77) were >18 years of age with severe hemophilia observed among majority (80.5%) of the patients.

In this study, arthropathy and hemarthrosis were the most common presentations with which the patients reported. Knee was the most common joint involved in 21 out of 66 patients (31.81%) who presented with complications. Gum bleed was present in 6.06%.In study conducted by Mishra et al[(17)], joint involvement was present in 77.9% of the patients. Knee joint was observed to be as the target joint among 57.1% of the patients. Bleeding occurred in soft tissues and joints in 62.3% and 15.6% of the patients, respectively. In Egyptian study by Tonbary el al[(18)], 22.2% patients had developed hemoarthrosis and only 9.7% patients were on orthophysiotherapy. One of them had permanent joint disability.

V. Conclusion

From the above study, we can fairly conclude that prevalence of hemophilia in northern India especially Punjab is significant enough to make it a disease of national concern. Also, the severe type of haemophilia type A is more common than mild and moderate types. Most patients usually present with complications like hemarthrosis and are diagnosed later. Most effective and easily available treatment available is specific factor replacement therapy. To improve the hemophilic care and early diagnosis, a multi-disciplinary approach is needed that includes training of care providers, setting up care centers, maintaining proper patient registry, educating patients and their families, providing low-cost factor concentrates. Since India lacks a national policy on the prevention and control of genetic disorders, this study also emphasizes the need to immediately initiate a national programme for haemophilia, with components of diagnosis, prevention, care and support.

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