ORIGINAL ARTICLE

Clinical Profile of Hemophilia in Children in a Tertiary Care Hospital in North India

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Abstract

Hemophilia is congenital X-linked disorder of the coagulation system whereby deficiency of factor VIII (hemophilia A) or factor IX (hemophilia B) predisposes the affected male to a lifelong risk of bleeds. Early and adequate support with factor replacement will prevent death from fatal bleeds. However, awareness levels among students and general practitioners continued to be very low resulting in delayed and inappropriate management. The present study designed to focus on the presentation, genetic aspects and management of hemophiliac children. Clinical profile of 119 diagnosed cases of hemophilia up to 18 years of age was analyzed. Out of a total 119 cases enrolled mean age of the patients was 9.5 years with an age range of 6 months to 18 years. 97(81%) cases were hemophilia A and 22 (18.4%) cases were hemophilia B. Only 48(40.0%) cases had family history of bleeding with 71 (60%) had no history of bleeding in family. Among the hemophilia A 50.4% (52.5%) cases had mild, 45.2 (47.5%) cases had moderate disease and among the hemophilia B, 9.5 (40%) cases had mild, 11.5 (50%) cases had moderate and 2.3 (10%) cases had severe disease. Hemarthrosis of knee joint was the major presentation followed by ankle, elbow, shoulder followed by circumcision and tooth extraction bleeding. 62% of the hemophiliacs in our study had initial bleeding episode before 1 year of age and by 6 years of age 94% of cases had developed symptoms of bleeding evidence. No patient had history of bleeding during neonatal period. It is concluded that hemarthrosis found to be the leading cause of presentation; bruises and hematomas either spontaneous or traumatic were the chief complaints at the presentation of these children.

Key Words

Hemophilia, X –linked recessive, Bleeding, Hemarthrosis

Introduction

Hemophilia A (factor VIII deficiency) and hemophilia B (factor IX deficiency) are the most common congenital coagulation factor deficiencies. The clinical findings in hemophilia A and hemophilia B are virtually identical. The inheritance is X-linked recessive, affecting the males; however, females are carriers (1,2,3). The main defect lies with the impairment of body's ability to form clot that is a natural process which enables to stop bleeding after trivial trauma, easy bruisability with an increased risk of spontaneous intra particular and intracranial hemorrhage (2). The overall prevalence is approximately 1 in 10000 individuals. The two most common forms are factor VIII deficiency or hemophilia-A, which comprises approximately 80% of cases and factor IX deficiency or hemophilia B, which comprises approximately 20% of cases (4,5). The incidence of hemophilia A (Classical) is 1: 5000 male births and that of hemophilia B (Christmas) disease is 1: 25000 (6). Approximately 30% of the patients have no family history and are as a result of denovo mutations on chromosome 4 (7). The defective gene is inherited in autosomal recessive manner meaning that both males and females have the same risk of inheriting the condition. For the disease to develop, a faulty copy of the gene must be inherited from each parent. The reduced level or activity of factor XI also known as hemophilia C or acquired hemophilia results in moderate bleeding symptoms usually occurring after trauma or surgery. The disorder can also occur if the body forms antibodies to

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own clotting factors in the blood that hampers the normal functioning of clot formation system (8).

Depending upon concentration levels of clotting factors disease is divided into: Mild that is more than 5 % but less than 40% (>0.05 <0.40 IU/mL), Moderate 1-5 (>0.01-<0.05 IU/mL) and Severe less than 1% (<0.01-<1 IU/mL) respectively (3,9). Severe and moderate hemophiliac might present at birth with prolonged bleeding from umbilical stump or intracranial hemorrhage (2,10). Serious intracranial hemorrhage (ICH) from trivial trauma endangers life of these severe hemophiliacs (11). Patients with mild and moderate disease generally bleed after significant trauma or surgical procedure rarely leads into recurrent hemarthrosis and consequently arthropathy, however patients with severe phenotype may bleed spontaneously or even after trivial trauma and consequently hemarthrosis and arthropathy (12,13). Prior to the availability of clotting factors concentrate most people with severe hemophilia developed crippling, musculoskeletal deformities and would have died due to hemorrhage (14).

In developing nations such as India, where patients with hemophilia have limited access to treatment and due to recurrent joint bleeds, there occur widespread disability and morbidity from joint impairment significantly with advancing age (15). In literature minimum research data is available with regards to hemophilia in children, which makes it very difficult to represent accurately the situation regarding epidemiology, clinical profile and diagnosis. By keeping in view this study was designed to observe the clinical presentation and management of hemophiliac children referred from various districts of the state to a "Comprehensive day Care hemophilia center" of a tertiary Care hospital in north India.

Material and Methods

The study has carried out in Hemophilia Care Centre that is a "Comprehensive Hemophilia Care Centre" in the department of Pediatrics, Govt. Medical College, Jammu. The subjects were the total 119 enrolled patients aged less than 18 years, occasionally attending hemophilia care center for factor replacement were included in the study. Detailed history of presentation regarding joint involvement for bleeding episodes during last one year and diagnosis at what age. Family history of bleeding as well as other associated symptoms and related complications were also recorded. Patients were also asked for any delay between onsets of 1st bleeding and definite diagnosis made to assess the gravity of awareness amongst medicos /health care provider about the hemophilia. All new cases were subjected to factor VIII and factor IX assay (if not previously done). Factor assay was done by one stage assay using "semiautomated clot analyzer". This is based on a comparison of the ability of dilutions of standard and test plasma to correct the activated partial thromboplastin time of plasma known to be totally deficient in factor VIII but containing all other factors required for normal clotting. Factor levels of 1%, 1-5% and 5-40% were defined as severe, moderate and mild hemophiliacs respectively. However, in old cases factor level were reconfirmed only in those cases where it had been done within 24 hours of receiving factor VIII, IX, blood products or in situation where "one stage assay" method was not employed for factor assay. Patients were also screened for any transfusion transmitted diseases like hepatitis B, hepatitis C, and HIV.

Inclusion criteria: All patients who were registered at Hemophilia Care Centre in the department of Pediatrics, Govt. Medical College Jammu as well as new cases included.

Exclusion criteria: Patients with congenital bleeding disorders other than factor VIII and factor IX deficiency and acquired bleeding disorders caused by drugs, infections, malignancies and platelet disorders were excluded from study.

In the statistical method, descriptive analysis of qualitative variables was expressed in frequency and percentages. Statistical average was done by mean value and dispersion measured by standard deviation.

Results

Among 119 patients of hemophilia studied, 80% were of hemophilia A and 20% hemophilia B.

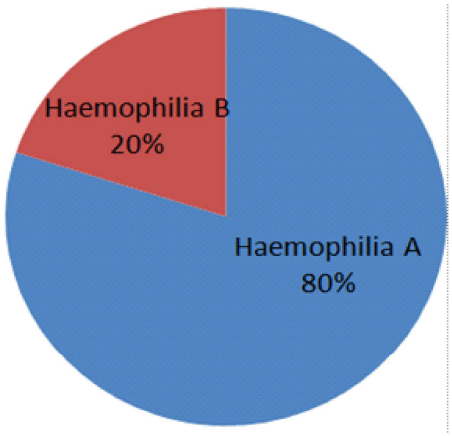

Fig. 1: Distribution of Patients by Types of Hemophilia

Table 1: Age Distribution of Patients with Hemophilia

Age Group	Type		Total Number (%)
	Hemophilia A	Hemophilia B	
Upto 6 Years	45 (37.45%)	13 (10.9%)	58 (48.7%)
7-12 Years	38 (31.93%)	9 (7.5%)	47 (39.4%)
13-18 Years	14 (11.78%)	0 (0)	47 (39.4%)

Table 2: Distribution of Hemophilia in Relation to Family History

	Frequency	Percent
Positive Family History	**48**	**40.0**
Other sibs	36	30.0
Maternal uncle	10	8
Maternal cousin	2.3	2
Negative Family History	**71**	**60**

Table 3: Distribution of Hemophilia According to Severity

Severity	Hemophilia A	Hemophilia B
Mild	50.4 (52.5)	9.5 (40)
Moderate	45.2 (47.5)	11.5 (50)
Severe	0 (00)	2.3 (10)

Table 4: Initial Presentation of Hemophilia

Features	Frequency	Percentage
Bruises and Ecchymoses	47.6	40%
Hemarthrosis	23.8	20%
Cut Injury to Lips and Chin	19.0	16%
Tongue Bite	19.0	16%
Gum Bleeding	4.7	4%
Circumcisional Bleeding	4.7	4%

Table 5: Frequency of Involvement of Joints

Involved Joints	Types		Total %
	Hemophilia A %	Hemophilia B%	
Knee	69 (58)	12 (10)	81 (68)
Ankle	42.8 (36)	9.5 (8)	52.3 (44)
Elbow	14.2 (12)	2.3 (2)	16.6 (14)
Shoulder	6.5 (8)	0 (0)	6.5 (8)
Others	3.5 (3)	0 (0)	3.5 (3)

Table 6: Complications of Hemophilia

Parameters	Types		Total %
	Hemophilia A %	Hemophilia B %	
Limitation of Movement of Joints	54.6 (46)	9.5 (8)	64 .26 (54)
Compartmental Syndrome	11.9 (10)	2.3 (2)	14.2 (12)
Intracranial Hemorrhage	0 (0)	2.3 (2)	2.3 (2)

Table 7: Age Distribution at Initial Presentation

Age Range	Frequency	Percentage
< 1 Year	73.78	62.0
1-6 Years	38.08	32.0
>6 years	7.14	6.0
Total	119	100

Discussion

We conducted an observational study in 119 patients diagnosed with hemophilia on the basis of factor VIII and IX assay's and described the clinical profile with respect to the age, gender and clinical signs and symptoms of these patients. The study conducted in a Tertiary Care hospital's Hemophilia Care Centre (SMGS-Hospital) in North India. Several important facts emerged from this descriptive study. The most important is the family history pattern i.e. in 48 (40%) patients out of 119 cases had significant positive family history of hemophilia. Out of these 36 (30%) patients had their siblings and 10 (8%) patients had their maternal uncle and only 2.3 (2%) with maternal cousins who were hemophiliacs in their families, whereas rest 71 (60%) patients had negative family history for hemophilia. Our results are comparable to the study of Rehman and Uddin *et al.* on Bangladeshi population (16). Our results are also matching with the results of Kar and Pontis-Lele's on Indian Hemophiliacs as well as Kim *et al.* on Korean Hemophiliacs (17,18). In our study, 58 (48.7%) patients were upto 6 years of age while 47 (39.4%) were between the age of 7-12 years and only 14 (11.47%) belonged to the age group of 13-18 years.

Majority of pediatric patients i.e. 94% have bleeding manifestations before 5 years of age (19), with mean age of onset ranging from 9 to 11 months depending upon

the severity (20). Initial bleeding site depends upon local factors. At a place where circumcision is a routine practice, post circumcision bleed has been found to be the most common initial bleed (51.4-62% of the case) (21,22). In our study post traumatic bleed has been found to be the most common initial (82%) manifestation. In the present study, 52.5% of Hemophilia-A and 40% of Hemophilia B had mild disease, 47.5% of Hemophilia A and 50% of Hemophilia B had moderate disease, and only 10% of Hemophilia B had severe disease. Similar result was reported by Rahman and Uddin *et al.* in two different studies on Bangladeshi people with 45% mild hemophilia and 42.5% with moderate hemophilia and 12.5% with severe hemophilia (16). Azhar *et al.* in their study on Spanish hemophiliacs and Nilsson in his study on Swedish hemophiliacs also showed higher percentage of mild cases (23,24). Joint bleed has been found to be the most common (82-100%) presenting feature followed by skin bleed (77-90%). In the present study hemarthrosis was the most common clinical manifestation, however a slightly lower frequency of hemarthrosis has been reported by Payal *et al.* in Hemophiliac pediatrics patients in Jodhpur, India (25). Among the joints affected, knee is most commonly involved in about 81 (68%) cases followed by ankle joint in 52(44%) cases, elbow joint in 16(14%) cases shoulder joint in 6 (8%) cases and other joint swellings were observed in 6% of cases. Similar results have been observed by Karim *et al.* in Bangladeshi hemophiliac children in tertiary care hospital (19). Similarly, more involvement of ankle joint was reported in a Pakistani study by Mohsin *et al.* (21). Majority 62% of the hemophiliacs in our study had initial bleeding episode before 1 year of age and by 6 years of age 94% of cases showed evidence of active bleeding but none of the cases had either any suspicion or any evidence in the neonatal period to think of in favor of hemophiliac bleeding this might reflect under diagnosis of hemophilia in our settings. While evaluating a case of bleeding neonate, a possibility of hemophilia should also be kept in mind despite the known fact that vit. K deficiency is far more common. Jamil *et al.* showed 64.3% cases with severe hemophilia detected at birth (26). Intracranial hemorrhage (ICH) with high potential for mortality and morbidity was observed in about 3-4% cases of severe hemophilia (27).

Conclusion

In the analysis of clinical presentation among pediatric age group hemarthrosis found to be the leading cause of presentation, bruises and hematomas either spontaneous or traumatic were the chief complaints at the presentation of these children. So, presence of these features in an otherwise normal child should be considered for the evaluation of hemophilia. Bleeding manifestations in newborn period and mimicking vitamin K deficiency warrant sincere vigilance evaluation of hemophilia in neonatal period, especially for ICH. By establishment of Comprehensive hemophilia care centers, specific training of medical and paramedical staff with promotion for regular availability of factor concentrate, prophylactic factor replacement therapy and effective and regular public awareness through print and media will augment in achieving the desired outcome in comparison with developed nation.

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