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Clinical Profile of Hemophilia in Children in a Tertiary Care Centre in Andhra Pradesh, India

KEYWORDS: Hemophilia, Bleeding disorder, Children, Hemarthrosis

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ABSTRACT ***Introduction:*** *Hemophilias are a group of inherited, life-long coagulation disorders. Hemophilia A (classic hemophilia, factor VIII deficiency) and hemophilia B (Christmas disease, factor IX deficiency) are sex-linked recessive disorders, with the incidence of hemophilia A outnumbering those with hemophilia B. Some of the patients have their disorder caused by mutation. Hemophilias are present in every nook and corner of the world and have a varied presentation. There is a high morbidity and mortality associated with it and knowing their presentation helps in better management practices.*

Objectives: *To observe the clinical presentation of hemophilia in children.*

Methodology: This observational study was carried out in the Department of Pediatrics, Alluri Sitarama Raju Academy of Medical Sciences for a period of one year from 1st February 2014 to 31st January 2015. Clinical profile of 66 diagnosed cases of hemophilia <15 years of age was analyzed.

Result: *All the cases under the study were male with an age range of 3 months to 15 years. Hemophilia A was seen in 51(77%) cases and 15(23%) cases were identified as hemophilia B. Only 49% cases had family history of bleeding. Among hemophilia A, 49% were mild, 39% were moderate and 12% with severe hemophilia. 53.34% of hemophilia B presented with mild disease, 33.33% with moderate form of the disease and 13.33% with severe disease. Hemarthrosis (68%) was the most common problem with which the patients presented. Gum bleeding was the second most common presentation followed by prolonged bleeding after tooth extraction, bruises and Ecchymosis. 49% of the patients had their first bleeding symptoms between ages of 1-5 years and 85 %cases showed bleeding manifestation before the age of 5. Only 15% cases had presented after 5 years of age. Bruises and hematoma were the most common initial manifestation followed by joint bleeding, cut injury of lips and chin, scalp and facial hematoma.*

Conclusion: *Bruises and hematoma were the main presentation features of the children in the study. Children with hemarthrosis have a rather morbid childhood. Cases as high as 36% of them presented before their first birthday which makes mandatory detection in infants.*

Introduction

Hemophilias are a group of inherited, life-long coagulation disorders. Hemophilia A (classic hemophilia, factor VIII deficiency) and hemophilia B (Christmas disease, factor IX deficiency) are sex-linked recessive disorders, with the incidence of hemophilia A outnumbering those with hemophilia B by a ratio of 4 or 5 to 1.About 30% of patients have their disorder caused by mutation (1). The reported hemophilia A prevalence in lower income countries is often considerably less than that in higher income countries, and less than expected from average international incidence. The literature (2-6) suggests that the incidence of Hemophilia is same for all populations and races and has been estimated to be 20 per 100 000male births (7,8). People with hemophilia registered in the Hemophilia Federation of India account for only about 10% of what is expected. There are many possible reasons for under reporting cases of hemophilia A. Aledort (9) reported that the majority of hemophiliacs in the developing world could not been identified because of a lack of diagnostic capability, lack of access to care and economic means, and unavailability of factor VIII replacement therapy. Without treatment, those with severe hemophilia often die in childhood or early adult life (10-13) thereby resulting in a decreased prevalence relative to the number of cases born. In addition, the reporting procedures in many countries have not accurately identified people with hemophilia. This study was designed to observe the clinical presentation of hemophilia in children in a tertiary care hospital which will provide glimpse of presentation of pediatric Hemophilia in the country.

Methodology

A cross sectional study was carried out on a total of 66 cases in the department of Pediatrics, Alluri Sitarama Raju Academy of Medical Sciences over a period of one year from 1st February 2014 to 31st January 2015. Hemophiliacs who were diagnosed earlier and suspected cases with bleeding disorders which afterwards were diagnosed as hemophilia either admitted into inpatient or attending at outpatient department of Pediatrics were included in the study. New cases of hemophilia who had received fresh frozen plasma, coagulation factors or cryoprecipitate within the timeframe of 24 hours were excluded from this study. Parents' consent was taken and history regarding presenting symptoms including symptoms at first presentation and family history were also taken. Parents were enquired about their child`s first bleeding presentation or was taken from the documents of the treating physicians. Evaluation of the symptoms was done through thorough physical examination. New cases were identified through investigations like complete blood count (CBC), prothrombin time (PT), activated partial thromboplastin time (APTT), factor VIII and IX assay. Reports of the CBC, PT, APTT and factors assay were collected from the patients who were diagnosed previously. Hemophilia diagnosis was made on the

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basis of prolonged APTT, and lower level of factor VIII and IX with normal PT and hemogram. The findings of the history, clinical examination and investigation were recorded in the semi structured questionnaires. Hemophilia A and B was defined as deficiency of Factor VIII and IX with < 30% of normal activity respectively. Mild, moderate and severe hemophilia were defined as factor level of >5-30%, 1-5 % and <1% of normal activity respectively.

Results

This study was done on 66 cases of hemophilia who were all males with the Mean age of the patients was 8.77 years with an age range of 3 months to 15 years. Age distribution of patient with hemophilia is clearly explained in table-1. Hemophilia A was seen in51 (77%) cases and 15 (23%) cases were identified as hemophilia B. Table-2 illustrates Family History of hemophilia according to which positive family history was seen in 49% of cases out of which 31% cases had affected brothers, 15 % cases had affected maternal uncle and 3% had affected maternal cousins.

Age Distribution of patient with hemophilia (table-1)

Age group	HemophiliaA(%)	HemophiliaB(%)	Total Number(%)
Up to 5	22(33)	8(12)	30(45)
6-10	16(24)	6(9)	22(33)
11-15	13(20)	1(2)	14(22)
Total	51(77.27)	15(23)	66(100)

Family History of hemophilia (table-2)

History	Frequency	Percent(%)
Positive Family History	32	49
Maternal Uncle	10	15
Other Siblings	20	31
Maternal Cousins	02	3
Negative Family History	34	51
Total	66	100

Table-3 clearly shows that among hemophiliaA, 49% were mild, 39% were moderate and 12% with severe hemophilia, and on the other hand 53.34% of hemophilia B presented with mild disease, 33.33% with moderate form of the disease and 13.33% with severe disease.

Distribution of Hemophilia according to severity (Table-3)

Severity	HemophiliaA(%)	HemophiliaB(%)
Mild	25(49)	8(53.34)
Moderate	20(39)	5(33.33)
Severe	6(12)	2(13.33)
Total	51(100)	15(100)

Hemarthrosis (68%) was the most common problem with which the patients presented. Gum bleeding (44%) was the second most common presentation followed by prolonged bleeding after tooth extraction in 21% cases at third. Bruises and Ecchymosis were seen in 15% cases. Hematuria and melena was seen in 5% cases. (table-4).

Presentation of Hemophilia (Table-4)

Features	Frequency	Percentage(%)
Joint Swelling	45	68
Oral and Gum Bleeding	29	44
Tooth Extraction	14	21
Bruises and Ecchymosis	10	15
Hematuria	3	5
Melena	3	5
ICH	1	2
Epistaxis	4	6
Scalp and Facial Hematoma	4	6

Knee joint swelling was present in 57.77% cases of Hemophilia A and 15.55 % cases ofHemophilia B. Ankle joint was involved in 42.22% cases of Hemophilia A and 8.88% cases ofHemophilia B, Elbow joint swelling was found in 15.55%of Hemophilia A and 2.22% cases of Hemophilia B.Shoulder joint and Hip joint involvement were 6.66% cases in cases Hemophilia A and hip joint involvement in case of Hemophilia B is 2.22% (table-5).

Frequency of Involvement of Joints (Table-5)

Joints	Hemophilia A	Hemophilia B	Total(%)
Knee	26(57.77)	7(15.55)	33(73.33)
Ankle	19(42.22)	4(8.88)	23(51)
Elbow	7(15.55)	1(2.22)	8(17.77)
Shoulder	3(6.66)	0	3(6.66)
Hip	3(6.66)	1(2.22)	4(8.88)
Others	2(4.44)	0	2(4.44)

In 68% cases of joint swelling, 49% cases showed limitation of movement of the affected joints, 38% in Hemophilia A and 11% cases in Hemophilia B and 12 % patients had compartmental syndrome in which 9 % cases in Hemophilia A and 3% cases in Hemophilia B. ICH was present in one patient with Hemophilia A(table-6).

Complications of hemophilia (Table-6)

Parameters	HemophiliaA(%)	HemophiliaB(%)	Total
Limitation of movement of joints	25(38)	7(11)	32(49)
Compartmental Syndrome	6(9)	2(3)	8(12)
ICH	1(2)	0	1(2)

And 49% of the patients had their first bleeding symptoms between ages of 1-5 years and cumulatively 85 %cases showed bleeding manifestation before the age of 5. Only 15% cases had presented after 5 years of age (table-7).

Age distribution at Initial Presentation (Table-7)

Age Distribution	Frequency	Percentage (%)
<1 year	24	36
1-5 years	32	49
>5 years	10	15

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Total	66	100

Most common initial presentation of the hemophiliacs as shown in table-8 was bruises and ecchymosis in 49% of cases that occurred spontaneously or following trauma. Hemarthrosis was the presentation in 18%cases and 14% cases showed cut injury to lips and chin. 11% cases presented with scalp and facial hematoma, gum bleeding (11%) and tongue bite (6%).

Initial presentation of Hemophilia (Table-8)

Features	Frequency	Percentage (%)
Bruises and Ecchymosis	32	49
Hemarthrosis	12	18
Cut injury to lips and chin	9	14
Scalp and Facial Hematoma	7	11
Tongue bite	4	6
Gum Bleeding	7	11

Discussion

Among the hereditary bleeding disorders hemophilia which is an X linked recessive disorder is very common and has variable clinical presentation depending upon the severity of the problem. Sixty six children with Hemophilia were studied to observe their clinical profile.

The present study shows the pattern of family history similar to the earlier study on Bangladeshi population by Rahman (14).Mac Lean et al. in their study in Netherlands showed although a positive family history was present in 52 gravidae, 16 of them (31%) were not aware of their carrier status at moment of delivery (15). So carrier detection might explore more family to be carrier of Hemophilia.

77% of the Hemophiliacs had Hemophilia A and 23% had Hemophilia B. Uddin et al. reported similar results in their study(14).Higher percentage of HemophiliaA which is about 85% is seen in the study on Korean people by Kim (16).

The present study shows 49% of Hemophilia A and 53% of Hemophilia B had mild disease, 39% of Hemophilia A and 33 % of Hemophilia B had moderate disease, and only 12 % of Hemophilia A and 13% of Hemophilia B had severe disease. As reported by Rahman and Uddin et al 45% mild Hemophilia, 42.5% moderate Hemophilia and 12.5 % severe Hemophilia (17,14). Studies done Kar and Pontis- Lele on Indian Hemophiliacs and Aznar et al on Spanish Hemophiliacs showed similar findings with higher percentage of mild Hemophilia. (18, 19).

Haemarthrosis was the most common presentation as observed in this study with68% cases followed by gum bleeding in 44% cases and excessive bleeding after tooth extraction in 21%cases. Korean nationwide study showed joint symptoms was the presenting sign in 81% cases followed by easy bruising, prolonged bleeding after trauma and soft tissue hematoma (16). In contrast Spanish Hemophiliacs reported arthropathy in less number of cases13.7% in Hemophilia A and 4.1% cases in Hemophilia B (19). The South African study showed subcutaneous hematoma was the leading symptoms for diagnosis in 51% cases of severe hemophilia and they reported only 5% cases with joint or muscle bleeding in severely affected cases, 21% cases in moderately affected and 9% cases in mild Hemophilia(20).

73% cases had knee joint as the most commonly affected joint followed by ankle joint swelling in 51%cases, elbow joint swelling in 17.77 % cases and shoulder joint swelling was present in 6.66% cases. Kim et al reported knee joint swelling in 84 % cases followed by ankle joint and elbow joint swelling in 21% and 22% cases respectively (16). The same study also shows that hip joint involvement was higher in 12.3% cases but wrist and shoulder joint involvement was low in 2.1% and 0.8% cases respectively (16). Higher frequency of ankle joint involvement was also reported by Molho et al. in Hemophiliacs in France (21). But Aznar et al. showed ankle joint was mostly affected after knee and elbow joint (19).

Initial presentation of the children with hemophilia was analyzed using the available physician's documents and parent's recall. Bruises and ecchymosis were the most common initial presentation in 49% of cases as per description of the parents. Joint swelling was present in 18% cases and gum bleeding was seen in 7% cases. Forty two percent cases had bleeding following some form of trauma such as tongue bite, gum bleeding and injury to lip or chin, tooth extraction, circumcision and scalp injury. James et al. reported initial presentation of Hemophilia children presented for evaluation of presumed coagulopathy where 35.7% of diagnosis of Hemophilia were made after positive family history, 32.1% after iatrogenic bleeding like circumcision, venipuncture and heal prick and the rest after spontaneous bleeding like bruising hematoma, cepalohematoma, gastrointestinal bleeding and ICH(22). Jamil et al. also studied initial presentation of severe Hemophiliacs and showed that circumcision being the most common cause of iatrogenic bleeding and bruising hematomas major cause of spontaneous bleeding (23).

49% of the hemophiliacs in this series had initial bleeding episode between the ages of 1 and 5 years and by the age of 5years 85% showed evidence of active bleeding. Jamesat el showed 64.2% cases with severe hemophilia presented with bleeding episode before 1 month of age (22). Bleeding following circumcision and venipuncture were the common presentation in the neonatal period. ICH with high potential for mortality and morbidity was observed in about 3-4% cases of severe hemophilia (24,25).

Conclusion

Hemarthrosis was the main morbidity of hemophilia in children in the present study but bruises and hematoma were the main features at initial presentation of these children. Great caution should be exercised for evaluation of hemophilia in a child with these features. About thirty six percent cases had presented before the age of one year which makes mandatory for more vigilance in detection of hemophilia in newborn and infants.

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REFERENCE

1)Kulkerni R, Lusher J. Perinatal management of newborn with hemophilia. Br J Hematol 2001; 112: 264-74 | 2) Bolton-Maggs PHB. Optimal haemophilia care versus the reality.Br J Haematol 2005; 132: 671–82. | 3) Chandy M. Management of haemophilia in developing countries with available resources. Haemophilia 1995; 1(Suppl 1): 44–8. | 4) Evatt BL. Demographics of hemophilia in developing countries. Semin Thromb Hemostasis 2005; 31: 489–94. | 5) Nathwani AC, Tuddenham EGD. Epidemiology of coagulation disorders. Baillie`re's Clin Haematol 1992; 5: 383–439. | 6) Srivastava A. Delivery of haemophilia care in the developing world. Haemophilia 1998; 4(Suppl 2): 33–40. | 7) Rosendaal FR, Brie¨t E. The increasing prevalence of haemophilia. Thromb Haemostasis 1990; 63: 145. | 8) Soucie JM, Evatt B, Jackson D, the Hemophilia Surveillance System Project Investigators. Occurrence of hemophilia in the United States. Am J Hematol 1998; 59: 288–94. | 9) Aledort LM. Unsolved problems in haemophilia. Haemophilia 1998; 4: 341–5. | | 10) Evatt BL. The natural evolution of haemophilia care: developing and sustaining comprehensive care globally. Haemophilia 2006;12(Suppl 3): 13–21. | 11) Skinner MW. Treatment for all: a vision for the future. Haemophilia 2006; 12(Suppl 3): 169–73. | 12) Ikkala E, Helske T, Myllyla¨ G, Nevanlinna HR, Pitka¨nen P, Rasi V. Changes in the life expectancy of patients with severe haemophilia A in Finland in 1930–79. Br J Haematol 1982; 52: 7–12. | 13) Larsson SA. Life expectancy of Swedish haemophiliacs, 1831– 1980. Br J Haemotol 1985; 59: 593–602. | 14) Uddin MM, Rahman MJ, Rahman MM, Sultana SA, Shah MS. Clinico-Pathological Study on haemophilia: An Analysis of 50 Cases. J Bangladesh Coll Phys Surg, 2006; 24: 50-53. | 15) MacLean PE, Fijnvandraat K, Beijlevelt M, Peters M. The impact of unaware carrier ship on the clinical presentation of haemophilia. Haemophilia 2004; 10: 560-64. | 16) Kim KY, Yang CH, Cho MJ, Lee M. Comprehensive clinical and statistical analysis of haemophilia in Korea 1988. J Korean Med Sc; 3: 107-14. | 17) Rahman M. Clinico-pathologic study on haemorrhagic disorder. (Dissertation) Dhaka, Bangladesh College of Physicians and Surgeons, 1998. | 18) Kar A and Pontis-Lele M. Descriptive epidemiology of haemophilia in Maharastra, India. Haemophilia 2001; 7: 561-567. | 19) Aznar JA, Lucia F, Abad-Frach L, Jimenez- Yuste V, Perez R, Bafle J et al. Haemophilia in Spain. Haemophilia 2009; 15: 665-75. | 20) Hazewinkel MH, Hoogerwarf JJ, Hesseling PB, Hertley P, MacLean PE, Peters M et al. Haemophilia patients aged 0-18 years in Western Cape. SAMJ. 2003; 13: 793-96. | 21) Molho P, Rolland N, Lebrun T, Dirat G, Courpied JP, Cronghs T et al. Epidemiological survey of the orthopaedic status of severe haemophilia A and B patients in France. Haemophilia 2000; 6: 23-32. | 22) Conway JH, Hilggatner MW, Initial Presentation of Pediatric Haemophiliacs. Arch Ped Adoles 1994; 148: 589-594. | 23) Jamil I, Bayoumy M, Iran D, Adler B. Pediatric severe Haemophilia: Initial presentation, characteristics and complications. The internet journal of Hematology 2004; 1 : ISSN 1540-2649. | 24) Ljung R, Chambost H Stain AM Dimichele D. Haemophilia in the first year of life. Haemophilia 2008; 14 (suppl 3): s188-195. | 25) Baehner RL and Strauss HS. Haemophilia in 1st year in life. N Eng J Med 1966; 275: 524-528.