

## CLINICAL PROFILE OF HAEMOPHILIA IN CHILDREN IN A TERTIARY CARE CENTRE

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### ABSTRACT

#### BACKGROUND

Haemophilia A and haemophilia B are the most common and serious congenital coagulation factor deficiencies. The clinical findings in haemophilia A and haemophilia B are identical. Majority of children with haemophilia show increased bleeding tendency by around one year. The hallmark of haemophilic bleeding is haemarthrosis.

#### MATERIALS AND METHODS

This is an observational study conducted at Government Medical College, Kottayam. Study population included all children with haemophilia less than 18 years of age attending the haemophilia clinic.

#### RESULTS

Total 40 children with haemophilia were enrolled in the study. Factor VIII deficiency was observed in 30 (75%) patients (Haemophilia A), while 10 (25%) patients were deficient in Factor IX (Haemophilia B). Majority of haemophilia patients in our study had severe deficiency.

#### CONCLUSION

Haemophilia A was more in our study. Bruises and ecchymoses are the most common initial presentation.

#### KEYWORDS

Haemophilia A, Haemophilia B, Inhibitors, Haemarthrosis, Factor Concentrate.

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#### BACKGROUND

Haemophilia A (factor VIII deficiency) and haemophilia B (factor IX deficiency) are the most common and serious congenital coagulation factor deficiencies. The clinical findings in haemophilia A and haemophilia B are identical.<sup>1</sup> Haemophilia occurs in approximately 1: 5,000 males with 85% having factor VIII deficiency and 10% - 15% having factor IX deficiency. A family history of bleeding is obtained in about two-thirds of patients with haemophilia. Females are usually carriers, transmitting the disease to their sons.<sup>2</sup> Depending upon the factor level, haemophilia is classified into mild (5% - 40%), moderate (1% - 5%) and severe (< 1%).<sup>3</sup> Characteristic clinical presentation of haemophilia is bleeding tendency. In severe haemophilia bleeding is spontaneous, whereas in moderate, prolonged bleeding with minor trauma and in mild bleeding occurs with major trauma or surgery.<sup>1,3,4</sup>

Although bleeding may occur in any area of the body, the hallmark of haemophilic bleeding is haemarthrosis. The earliest joint haemorrhages appear most commonly in the ankle. In the older child and adolescent, haemarthroses of the knees and elbows are also common.<sup>1</sup> A target joint is a joint in which 3 or more spontaneous bleeds have occurred within a

consecutive 6-month period. Recurrent bleeds into joints and muscles can lead to haemophilic arthropathy and contractures.<sup>5</sup> Intracranial, neck/throat or gastrointestinal haemorrhages are considered to be serious and life-threatening.<sup>4,6</sup> Other sites of bleeds are skin, gum, nose and genitourinary tract.

Early recognition and proper treatment of bleeds are important for the prevention of progressive disability. The bleeding episodes are treated with factor replacement therapy with either factor VIII for haemophilia A and factor IX for haemophilia B or with cryoprecipitate or fresh frozen plasma.<sup>7,8</sup> Of these, clotting factor concentrate is the preferred treatment option. But its most important complication is the development of inhibitors, which can neutralise the clotting factors.<sup>9</sup> Another complication is transfusion related infections like HIV, Hepatitis B and C etc.<sup>10</sup>

Haemophilias are distributed worldwide and have heterogeneous presentation depending upon its severity. India has a very large population of patients with haemophilia; 15,000 - 16,000 persons with haemophilia are registered with the Haemophilia Federation of India.<sup>11</sup> The present study was undertaken to identify the clinical presentation of haemophilia in children. Increased awareness among medical professionals about the varying clinical presentation of haemophilia can help in early diagnosis and management, thus preventing progressive disability and mortality.

#### MATERIALS AND METHODS

This is an observational study conducted at Government Medical College, Kottayam. The study was approved by the Institute of Research and Ethical Committee. Study

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population included all children with haemophilia less than 18 years of age attending the haemophilia clinic. An informed written consent was obtained first. A detailed history including patient's demographic data, type of haemophilia, severity, mode of presentation, past treatment and bleeding episodes, previous investigation reports, family history, age of onset of the disease, associated symptoms, complications and treatment history was taken. A thorough clinical examination was performed on these patients. All the results were entered on SPSS 16.0 for further analysis. Data were analysed by using SPSS statistical software (statistic package of social sciences) version 14.01 to obtain frequency tables and cross tabulation with figures to illustrate the results.

**RESULTS**

Total 40 children with haemophilia were enrolled in the study. Out of this factor VIII deficiency was observed in 30 (75%) patients (Haemophilia A), while 10 (25%) patients were deficient in Factor IX (Haemophilia B); 35 children were having severe haemophilia, whereas 5 children were moderate haemophiliac (Table 1). There were 6 children below 5 years, 15 children between 6 - 12 years, 19 children above 12 years (Table 1). Majority (47.5%) had their first bleed during 1 - 5 year period; 16 (40%) children developed their first clinical symptom during infancy. Most common type of first episode of bleeding observed was bruises and ecchymotic patches. Only 5 (12.5%) cases presented after 5 years of age (Table 3).

Table 4 illustrates the family History of haemophilia according to which positive family history was seen in 67% of cases. Most common type of bleed observed was joint bleed (57.5%) followed by bruises and ecchymosis (Table 5). Most common joint affected was knee followed by ankle; 10 children had haemophilic arthropathy characterised by pain and limitation of movement. Life threatening bleeds like intracranial bleed occurred in six children and fortunately all survived. Regarding the inhibitor status, 2 out of 40 children were found to be inhibitor positive (Table 6). None had transfusion related illnesses like HIV, HCV or Hepatitis B.

Type	Moderate	Severe	Total
Haemophilia A	3	27	30(75%)
Haemophilia B	2	8	10(25%)
<b>Total</b>	<b>5 (12.5%)</b>	<b>35 (87.5%)</b>	<b>40</b>

**Table 1. Distribution of Haemophilia according to Severity and Types**

Age	Haemophilia A	Haemophilia B	Total
Up to 5 years	3	3	6(15%)
6 - 12 years	12	3	15(37.5%)
> 12	15	4	19(47.5%)

**Table 2. Age Distribution of Patient with Haemophilia**

Age of First Presentation	Haemophilia A	Haemophilia B	Total
< 1 year	13	3	19(40%)
1-5 year	14	5	16(47.5%)
> 5 years	3	2	5(12.5%)

**Table 3. Age of First Presentation**

Features	Frequency	Percentage
Bruises and ecchymosis	22	55%
Haemarthrosis	12	30%
Scalp/ facial haematomas	3	7.5%
Prolonged bleeding from wounds	3	7.5%
Gum bleeding	2	5%

**Table 4. Initial Presentation of Haemophilia**

Family History	Yes	No
Haemophilia A	18	12
Haemophilia B	6	4
<b>Total</b>	<b>24(60%)</b>	<b>16(40%)</b>

**Table 5. Family History**

Type of Bleed	Frequency	Percentage
Joint bleed	23	57.5%
Bruises and ecchymosis	11	27.5%
Gum bleed	2	5%
Haematoma scalp/ face	2	5%
Muscle bleed	2	5%

**Table 6. Most Common Type of Bleeding**

Parameters	Haemophilia A	Haemophilia B	Total
Joint deformity	7	3	10(25%)
Intracranial bleed	4	2	6(15%)
Inhibitor	2	0	2(5%)

**Table 7. Complications of Haemophilia**

**DISCUSSION**

In our study, majority (75%) of children were found to have Haemophilia A and only (25%) were having Haemophilia B. This is similar to the study done by Mishra et al, who observed haemophilia A (88.3%) was the most common type of haemophilia as compared to haemophilia B.<sup>12</sup> Agarwal et al<sup>13</sup> also found the percentage of haemophilia A being 78.6% (236/ 300 cases). Kulkarni et al states that majority (81%) of their haemophilia patients belonged to Haemophilia A and only 19% were having haemophilia B.<sup>14</sup> Majority of haemophilia patients in our study had severe factor deficiency, which is similar to the findings reported by Parthiban et al<sup>15</sup> in which both haemophilia A and B showed 66% of cases with severe factor deficiency, 26% with moderate and 8% with mild deficiency. Our findings of severity of haemophilia are also in correlation with Agarwal et al.<sup>13</sup> The family history was present among more than half of the patients in this study. Similar percentage was reported by Parthiban et al,<sup>15</sup> in which 52.2% of the patients had family history.

In our study 40% of children presented in infancy, 47.5% presented between 1 and 5 years and 12.5% presented after 5 years. But James et al showed 64.2% cases with severe haemophilia presented with bleeding episode before 1 month of age.<sup>16</sup> We observed bruises and ecchymosis were the most common initial presentation. In our study, haemarthrosis was the most common (57.5%) type of bleeding followed by skin and subcutaneous bleeds. In an Indian study by Kar et al<sup>17</sup> in 148 patients with severe haemophilia A, knee joint was affected in all. The long-term consequences of repeated joint bleeds are the development of progressive joint damage and disability.<sup>18</sup> We also observed haemophilic arthropathy in 10 children. One of the complications of replacement therapy is

the development of alloantibodies called inhibitors, which can neutralise clotting factor concentrate.<sup>19</sup> In our study, 2 (5%) out of 40 children were found to have inhibitor. A systematic review reported the prevalence of patients with inhibitors between 5 to 7 percent with the risk of inhibitor development being higher in patients with severe rather than mild or moderate haemophilia A.<sup>20</sup> Though patients with haemophilia are vulnerable to transfusion transmitted infections, none of our study population had the same.

### CONCLUSION

Haemophilia A was more in our study. Bruises and ecchymoses are the most common initial presentation and majority of children had their first bleed during 1 - 5 year period. Haemophilia is still not a disease of public health relevance in India like other developed countries. There is very little information on the disease and its varying clinical presentation in our society. But for the persons affected, this is a lifelong problem. So there is a dire necessity to create awareness about this disease among general practitioners as well as general population, so that patients can be referred early to the haemophilia centres.

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