



Study of bleeding disorders (hemophilia) in children in Beni-Suef university hospital

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Abstract:

The goal of this study is to study the clinical spectrum of hemophiliac children (age <18 years) in Beni-Suef university hospital. A cross-sectional study conducted in the pediatric hematology clinic of Beni-Suef university hospital, over a period of 12 months. Out of a total of 112 cases enrolled, 91% were diagnosed as hemophilia A. While (9%) were diagnosed as hemophilia B. Positive family history was found in (46%) of cases. The mean age of onset of symptoms and diagnosis was 1.7 ± 1.4 and 3.8 ± 3.8 years, respectively.), the most common bleeding symptom was bruises (86.5), the most serious was intracranial hemorrhage (9.6%). While haemarthrosis was in (7.7%). Conclusion: Occurrence of posttraumatic bleeds and gum bleeds in an otherwise normal child should warn the clinician for evaluation of hemophilia. Hemophilias are distributed worldwide and have heterogeneous presentation depending upon the disease severity. Knowledge of the spectrum of presentation of hemophilia in the local population helps in early diagnosis and planning of management.

Keywords: Cross section study, hemarthrosis, hemophilia.

1. Introduction:

Hemophilia types A and B are inherited diseases. They are passed on from parents to children through a gene on the X chromosome. Females have two X chromosomes, while males have one X and one Y chromosome. In about one-third of the children with hemophilia, there is no family history of the disorder. In these cases, it's believed that the disorder could be related to a new gene flaw.

Carriers of the hemophilia gene often have normal levels of clotting factors but may: bruise easily, bleed more with surgeries and dental work, have frequent nosebleeds and have heavy menstrual bleeding [1,2]. The most common symptom of this disorder is heavy, uncontrollable bleeding.

The severity of hemophilia depends on the amount of clotting factors in the blood. Those

affected with hemophilia that have levels greater than 5% (100% being average for unaffected children) most often have bleeding only with major surgeries or tooth extractions. These children may not even be diagnosed until bleeding complications from a surgery occur.

Severe hemophilia is when the factor VIII or IX is less than 1%. Bleeding can occur in these children, even with the minimal activities of daily life. Bleeding may also occur from no known injury. Bleeding most often occurs in the joints and in the head [3,4]. Diagnosis of hemophilia is based on your family history, your child's medical history, and a physical exam. Blood tests include: Complete blood count (CBC). A complete blood count checks the red and white blood cells, blood clotting cells (platelets), and sometimes, young red blood cells (reticulocytes). It includes hemoglobin and hematocrit and more details about the red blood cells. Clotting factors. To check the levels of each clotting factor. Bleeding times. To test the speed that blood clots. Genetic or DNA testing. To check for abnormal genes [5]. Treatment depends on the type and severity of the hemophilia. Treatment for hemophilia is aimed at preventing bleeding complications (mainly head and joint bleeds). Treatment may include: Bleeding in the joint may need surgery or immobilization. Your child may need rehab of the affected joint. This may include physical therapy and

exercise to strengthen the muscles around the area. Blood transfusions may be needed if major blood loss has occurred. This is when your child gets donated blood. Self-infused factor VIII or IX can allow a child with hemophilia to lead a near normal lifestyle [6]. Complications of hemophilia include: Bleeding in the joints or muscles Inflammation of the joint lining. Long-term joint problems. Very serious tumor-like enlargements, of the muscle and bone. Development of antibodies against clotting factors. Infections from transfusions (HIV and hepatitis B and C are no longer transmitted in donated blood) [7].

2. Patients and Methods:

A cross-sectional study conducted in the pediatric hematology clinic of Beni-Suef university hospital, over a period of 12 months. A total of 122 diagnosed cases of hemophilia (diagnosed by factor assay) aged <18 years were included in the study.

A detailed history was recorded regarding family history, age of first bleed, site of first bleed, age of diagnosis, bleeding history of last 1-year, age of first joint bleed, most affected joints in decreasing order of frequency, treatment type, and treatment products used. All new cases were subjected to factors VIII and IX assay (also if not previously done). In old cases, factor level were reconfirmed only in cases where it had been done within 24 h of receiving factor VIII/IX or blood products or method employed was not one-stage assay. Factor assay was done by using semi-

automated clot analyzer. This is based on a comparison of the ability of dilutions of standard and test plasmas to correct the activated partial thromboplastin time of plasma known to be totally deficient in FVIII but containing all other factors required for normal clotting.

2.1 Inclusion criteria:

- Patients < 18 years.

2.2 Exclusion criteria:

- Patients > 18 years.

Statistical methodology:

Statistical analysis was done using the statistical package for the social sciences (SPSS version 22.0) (IBM Corp, NY, USA). Data were expressed as (mean \pm SD) for quantitative data and qualitative data were presented as frequencies and proportions. Differences between the groups were analyzed using Student's t-test and ANOVA tests as regard normally distributed data. The Chi-square test was used to compare ratios. SNP genotypes and alleles analysis was done using the online SNP state program. P-value < 0.05 was considered statistically significant.

3. Results:

Out of a total of 112 cases enrolled, 91% were diagnosed as hemophilia A. While (9%) were diagnosed as hemophilia B. Positive family history was found in (46%) of cases. The mean age of onset of symptoms and diagnosis was 1.7 ± 1.4 and 3.8 ± 3.8 years, respectively.

In the study group, majority (40.85) of cases belonged to 1-5 years age group, followed by 34% cases in 5-10 years age group, and the mean age of studied group was 5.8 ± 3.5 years. Three patients (5.35%) had their onset of symptoms prior to 1-month but none was diagnosed in that period. Similarly, by 5 years of age though majority (83%) had experienced symptoms but only 67% were diagnosed by that time. Mean age of onset of symptoms was 1.73 ± 1.43 years while mean age of diagnosis was 3.5 ± 3.8 years

Frequency of bleeding symptoms in the study group was demonstrated in (table 1), the most common bleeding symptom was bruises (86.5), the most serious was intracranial hemorrhage (9.6%). While haemarthrosis was in (7.7%).

Table 1: Clinical manifestation of hemophilia

| Symptoms | Number | Percentage |
|----------------------------------|--------|------------|
| Epistaxis | 66 | 63.5% |
| Petechiae | 60 | 57.7% |
| Bruises | 90 | 86.5% |
| Haematuria | 12 | 11.5% |
| Haematemesis | 12 | 11.5% |
| Bleeding per rectum | 14 | 13.5% |
| Gum bleeding | 64 | 61.5% |
| Bleeding with tooth eruption | 10 | 9.6% |
| Bleeding with tooth extraction | 32 | 30.8% |
| Muscle haematoma | 54 | 51.9% |
| Haemarthrosis | 8 | 7.7% |
| Intracranial haemorrhage | 10 | 9.6% |
| Umbilical stump bleeding | 20 | 19.2% |
| Postcircumcision bleeding | 14 | 13.5% |
| Bleeding from IM injection sites | 2 | 1.9% |
| Subconjunctival haemorrhage | 4 | 3.8% |

Table 2: Laboratory data of the study group

| Std. Deviation | Mean | Maximum | Minimum | |
|----------------|----------|---------|---------|-----------------------------------|
| 112.49361 | 319.2222 | 676.00 | 129.00 | Platelet count (mm ³) |
| 1.52086 | 10.4669 | 12.50 | 3.30 | Hb (gm/dl) |
| 3.57378 | 8.9076 | 23.40 | 3.80 | WBCS (mm ³) |
| 5.225 | 4.07 | 35 | 1 | Bleeding time (minute) |
| 11.28079 | 18.4059 | 50.00 | 10.40 | PT (second) |
| 27.48929 | 81.8472 | 112.00 | 12.50 | PC (%) |
| 1.44319 | 1.8309 | 7.60 | 95. | INR |
| 37.57899 | 50.6889 | 172.00 | 30.00 | PTT (second) |

(46.42%) had 1-5 bleeding episodes in the last 1-year. (14.28%) had >10 bleeds in the last year. The mean annual number of bleeds was 6.5 ± 9 /year. (53.57%) developed 1-5 joint bleeds in the last 1-year. More than 10 bleeds were present in (7.14%) of cases.

All patients had received episodic treatment. A maximum of (80%) of patients had received cryoprecipitate, (70%) had fresh frozen plasma, and (45%) had clotting factors. Whole blood was transfused in (43%) of cases.

4. Discussion:

Hemophilia A is more common than hemophilia B. In most of the studies, hemophilia A constituted around 80% of total hemophilias [8,9,10,11,12]. In Pakistani population, proportion of hemophilia A was found to be low (65%) [13], in contrast in our study, it was slightly higher than previous studies (91% vs. 80%). Based on severity, hemophilia is further classified into mild, moderate, and severe, last one being the most prevalent with its proportion ranging from 43% to 55.7% [12,14,15,16]. In the present study also, severe was the most prevalent (44.64%), and mild was the least prevalent (19.64%). In a striking contrast in Bangladesh, mild variety was found to be the most prevalent [8,9].

Being an inherited disorder, family history has been observed in 40-71% cases of hemophilias [9,10,13,16]. In our study also, it was positive in 46.42% cases. Majority of pediatric patients (94%) has bleeding manifestations before 5 years of age [9] with mean age of onset ranging from 9 to 11 months depending upon the severity [14]. In our study also, 93% had their onset before 5

years of age with the mean age of onset of symptoms being 1.73 ± 1.43 years. Despite early age of onset (<5 years), only 65-73% are diagnosed till 5 years of age [13,17]. In the

present study, this percentage was slightly higher (77%) with mean age of diagnosis being 3.87 ± 3.84 years.

Initial bleeding site depends upon local factors. At a place where circumcision is a routine practice, postcircumcision bleed has been found to be the most common initial bleed [13,18]. Barring this, posttraumatic bleed has been found to be the most common initial manifestation of hemophilias [13,18] as in our study also, it was observed in 36% of cases.

Joint bleed (hemarthrosis) has been found to be the most common presenting feature followed by skin bleeds (77-90%) [8,9,16,19].

In the present study, bruises and epistaxis were the most common clinical manifestations. While hemarthrosis in 7.7%, our study was restricted to pediatric subjects only, and this may be the reason of slightly lower frequency of hemarthrosis. Among the joints affected, knee is the commonest followed by elbow and

ankle joints [9,20]. In our study also, knee joint was predominant but ankle joint was more common than elbow joint. Similarly, more involvement of ankle joint was reported in a study in Bangladesh [13]. Our results may be due to more involvement of knee joint with an abnormal gait, which predispose to repetitive ankle hemarthrosis or may be due to higher physical activity due to lack of public awareness for hemophilia in our setup.

All patients had received episodic treatment. A maximum of (80%) of patients had received cryoprecipitate, (70%) had fresh frozen plasma, and (45%) had clotting factors. Whole blood was transfused in (43%) of cases.

In Western studies, use of factor concentrates range from 74% to 100% [12,14,30]. In the present study, only 45% had received factors. In our study, low factor transfusion rates are attributed to the poor economic status of the patients who could not afford factor replacement therapy.

5. Conclusion:

Hemophilias are distributed worldwide and have heterogeneous presentation depending upon the disease severity. Knowledge of the spectrum of presentation of hemophilia in the local population helps in early diagnosis and planning of management.

Conflicts of interest:

There are no conflicts of interest.

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