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Clinico-Pathological Study on Haemophilia: An Analysis of 50 Cases

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Summary:

A prospective study was carried out on the patients presenting with history of recurrent joint swelling and wound bleeding in outpatient department of Haematology, Bangabandhu Sheikh Mujib Medical University (BSMMU) and Armed Forces Institute of Pathology (AFIP), Dhaka Cantonment from January 2000 to December 2000. Fifty patients were studied. The predominant age group affected were between six and 15 years (44%). Recurrent joint swelling was the predominant presenting symptom (100%) followed by wound bleeding (52%) and bleeding after tooth extraction (38%). Thirty (60%) patients had positive family history of bleeding. Coagulation screening tests showed that 40 (80%) patients had prolonged activated partial thromboplastin time (APTT). Amongst these 40 patients, 32 (80%) were diagnosed as haemophilia-A and eight (20%) as haemophilia-B. Eighteen (45%) patients had mild haemophilia, 17 (42.50%) moderate haemophilia and five (12.50%) patients had severe haemophilia. Spontaneous bleeding history was present in seven (17.50%) patients, and 16 (35.50%) patients with moderate haemophilia and 17 (47%) patients with mild haemophilia had bleeding following trauma or surgery.

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Introduction:

Inherited disorders of coagulation usually are the result of a deficiency or abnormality of a single plasma protein. As a consequence, these disorders provide a unique opportunity to study the phenomena of blood coagulation. With the exception of Von Willebrand's disease, the inherited coagulation disorders associated with bleeding produce similar signs and symptoms, regardless of the particular factor that is lacking[1].

A severe and often fatal haemorrhagic diathesis that affected the male children of certain families recognized in antiquity. This is evident from the writings of Rabbi Simon ben Gamaliel (Second century AD) in the Thalmud, and those of Maimonides, the Hebrew physician and philosopher, and Albucasis, the Arab (Twelfth century)[2,3].

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Haemarthrosis is the most common, the most painful, and the most physically, economically, and psychologically debilitating manifestation of the inherited coagulation disorders, especially haemophilia A[4,5]. The aim of this study was to find out the incidence of haemophilia among the patients presented mainly with recurrent joint swelling and to compare the findings with other studies of similar nature.

Materials and method:

This study was conducted in the Department of Haematology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka and Armed Forces Institute of Pathology (AFIP), Dhaka Cantonment during the period of January 2000 to December 2000. Fifty patients attending with history of recurrent joint swelling, wound bleeding, and prolonged bleeding after tooth extraction and circumcision in out-patient department were included in this study. A thorough history including family history and physical examination was done in every case. Diagnosis was made on the basis of history, physical examination and laboratory investigations such as bleeding time (BT), clotting time (CT), prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin time (TT) and coagulation factor assay such as factor VIII and factor IX. BT was measured by Ivy's method. Nine volume of blood (4.5 ml) was

added to one volume of 3.8% trisodium citrate (0.5 ml) in a plain test tube to measure PT, APTT, TT and coagulation factor assay was done by semi-automated coagulometer. Complete blood counts including peripheral blood smears were also made to see blood cell morphology and platelet count. Results of the investigations were recorded and analyzed.

Results:

In this study, 50 cases attending with a history of recurrent joint swelling, wound bleeding and prolonged bleeding after tooth extraction and circumcision in the Department of Haematology, BSMMU and AFIP, Dhaka Cantonment were included. The predominant age groups affected were between six and 15 years (44%) (Table-I). Recurrent joint swelling was the predominant presenting symptoms (100%) followed by wound bleeding (52%), bleeding after tooth extraction (38%), bleeding after circumcision (18%) and signs of arthritis (40%) (Table-II). The patients had more than one symptom. Thirty (60%) patients had positive family history of bleeding (Table-III). Complete blood count and X-ray of the affected joint of all patients were done. Out of 50 patients, 40 patients had positive findings in X-ray which was characteristic of chronic Haemarthosis. Complete blood count was found almost normal in every case. Results of coagulation screening tests showed that 40 (80%) patients had prolonged APTT and 10 (20%) had normal screening tests. So, 40 patients had been suffering from inherited coagulation disorders (Table-IV). Reduced activity of factor's VIII and IX was observed in 32 (80%) and in eight (20%) patients respectively. So, amongst 40 patients having prolonged APTT, 32 cases were diagnosed as haemophilia A and eight cases as haemophilia B (Table-V). Eighteen (45%) cases had mild haemophilia, 17 (42.50%) moderate haemophilia and five (12.50%) cases were diagnosed as severe haemophilia (Table-VI). Spontaneous bleeding history was present in all severe haemophilic patients and two patients with moderate haemophilia (17.50%). Sixteen (35.50%) patients with moderate haemophilia and 17 (47%) patients with mild haemophilia had bleeding following trauma or surgery (Table-VII).

Table-I

Age distribution of the patients (n=50)

Age (years)	Number of patients (%)
0-5	09 (18)
6-15	22 (44)
16-30	19 (38)

Table-II

Signs and symptoms of the patients (n=50)

Signs/Symptoms	Number of patients (%)
Joint swelling	50 (100)
Wound bleeding	26 (52)
Bleeding after tooth extraction	19 (38)
Bleeding after circumcision	09 (18)
Signs of arthritis	20 (40)

* The patients had more than one symptom.

Table-III

Results of coagulation screening tests (n=50)

Name of the test	Result	Number of patients (%)
Bleeding time (BT)	Normal	50 (100)
Coagulation time (CT)	Prolonged	40 (80)
Prothrombin time (PT)	Normal	50 (100)
Activated partial thromboplastin time (APTT)	Prolonged	40 (80)
Thrombin time (TT)	Normal	50 (100)
Platelet count	Normal	50 (100)

Table-IV

Results of the factor assay (n=40)

Factor VIII level	Factor IX level	Number (%)
Reduced	Normal	32 (80)
Normal	Reduced	08 (20)

Table-V

Severity of haemophilia (n=40)

Factor activity (Normal level Factor VIII and IX l 60%-150%)	Number of patients (%)
Mild (6-30%)	18 (45)
Moderate (1-5%)	17 (42.5)
Severe (<1%)	05 (12.5)

Table-VI

Type of bleeding among the hemophilic patients (n=40)

Type of bleeding	Number (%)
Spontaneous bleeding	07 (17.5)
Bleeding following trauma/ surgery	33 (82.5)

Discussion:

After initial coagulation screening tests, out of 50 cases 10 cases were excluded from the study because of negative screening tests.

Regarding age distribution of the patients, 22 (44%) patients presented with symptoms in the age group of 6-15 years and 19 (38%) in the age group 16-30 years in this study. Salim's study showed 71.4% patients presented with symptoms after the age of six years. This difference may be due to the inclusion of paediatric groups in that study[7].

Recurrent joint swelling was the predominant clinical finding followed by wound bleeding in this study. Although recurrent joint swelling was present in 100% cases but chronic haemarthosis characteristic of joint bleeding was present in 80% cases, which is almost similar to two previous studies[6,7]. Salim in another study found haemarthosis only in 42.8% cases[8]. The reason for this difference of joint bleeding with the latter study may be due to restriction of study on children only. The increased incidence of joint bleeding in this series may be due to the inclusion of mainly referred cases presenting with recurrent joint swelling.

The incidence of wound bleeding in this study was 52%. In two another studies, wound bleeding was found in 45.50% and 43% cases, which are almost similar to this study[6,8]. Hoyer found wound bleeding in 48% cases[9]. Other symptoms such as bleeding after tooth extraction and bleeding after circumcision were present in 38% and 18% case respectively in this study, which is similar to Gilbert's study[10]. Roberts found bleeding after tooth extraction in 42% cases and bleeding after circumcision in 20.20% cases[11]. Salim AFM's study showed bleeding after tooth extraction in 24.80% cases which differs from this study and also from Roberts's study.

This study showed that out of 50 patients, 30 (60%) had positive family history of bleeding, whereas Salim found 57.50% patients had positive family history of bleeding and Rahman in another study showed 55.50% cases to have positive family history of bleeding[6,8]. Amongst the relatives, history of bleeding was found in maternal uncles, brothers and cousins in studies. These findings are almost similar to this present study.

In this study, complete blood count and X-ray of the affected joint of all patients were done. Out of 50 patients, 40 patients showed changes in X-ray, which is characteristic of chronic haemarthosis. Coagulation profiles were done in 50 patients, 40 (80%) patients showed prolonged APTT and 10 (20%) showed normal results. Out of 40 patients having prolonged APTT, 32 (80%) cases were diagnosed as haemophilia A and eight (20%) cases as haemophilia B. Rahman's study showed almost the similar incidence of haemophilia A (80%) and haemophilia B (20%)[6]. Pasino et al, also showed almost similar incidence of haemophilia A and haemophilia B[12].

Mild haemophilia was found in 18 (45%) cases whereas moderate and severe haemophilia were found in 17 (42.50%) and five (12.50%) cases respectively. These findings are almost similar to those of Rahman who found 45.50% cases as mild, 45.50% as moderate and 9% cases as severe haemophilia[6]. But in another study, Rodgers found 20% cases as mild, 30% as moderate and 50% cases as severe haemophilia[1]. The reason of increased incidence of severe haemophilia in Rodgers study is difficult to interpret but may be due to more indepth investigations.

Spontaneous bleeding history was present in all severe haemophilic patients and two (11.7%) patients

with moderate haemophilia, and no history of spontaneous bleeding was found in mild haemophilia in this study. Railton found 98.2% cases of severe haemophilia to have spontaneous bleeding, and 7.4% cases of mild haemophilia had spontaneous bleeding and 40 % cases had bleeding after trauma[13]. Lusher in another study found 84% cases of severe haemophilia and 8% cases of moderate haemophilia to have spontanues bleeding[14]. These findings are almost similar to this present study.

Bleeding after injury is an everyday experience for healthy people and it can be very difficult to decide whether or not apparently excessive bleeding is due to a blood disorder. Serious congenital conditions, such as severe haemophilia, usually become obvious in early childhood but can be misdiagnosed as non-accidental injury. Milder bleeding disorders can remain undetected into old age, especially in those who have not undergone surgery in earlier adult life. It is the frequency and persistence of blood loss together with the minimal severity of injury required to produce it which should alert the physician to the likelihood of a haemostatic defect, while volume of loss is a poor guide.

Haemophilia A has been recognized in all areas of the world where adequate information is available. In Bangladesh, a number of studies were carried out on haemorrhagic disorders including haemophilia. In this study an attempt has been made to find out the incidence of haemophilia among those presented with the history of recurrent joint swelling, and to compare the clinical and laboratory findings with other studies of similar nature. However, more extensive studies of similar nature should be done in this country to generate a better result.

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