

Emergencies in People with Hemophilia (PWH)

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ABSTRACT

Introduction: PWH will present with various bleeding emergencies. Management in resource poor setting is a challenge because majority cannot afford. Situation warrants usage of factor concentrates in minimum effective thrombotic doses. Current study aimed to see the various emergencies encountered in PWH.

Material and Methods: We retrospectively collected data from case records of people with Hemophilia (PWH) who presented with bleeding emergencies over a period of one year. And the parameters studied were Age, symptoms, signs, risk factors, investigations like ultrasound, CTScan, clotting factor assay, inhibitors, screening for transmitted infections like HIV, Hepatitis C, Hepatitis B were done, treatment extended and outcome.

Results: Total 66 of PWH came with bleeding episodes in 1 year to emergency department. Average age was 23.95 years. Hemophilia A in 58 and 8 were hemophilia B. Average body weight was 48.3kgs. Mild hemophiliacs were 6, moderate 27 and severe 33. Spontaneous bleeding episodes were noted in 44. Precipitating factors for bleeding were noted as injury in 14, intra-muscular injection 2, infection 2, tooth extraction, boil, and seizures in 1 each. Average duration of bleeding was 1.4 days.

Conclusion: Minimum effective factor concentrates can bring gratifying results in majority. In certain situations higher doses are needed to stop the bleeding. Activated factor VII is an effective alternative in some PWH with inhibitors.

Keywords: Hemophilia, Arthropathy, Bleeding, Inhibitors

INTRODUCTION

Hemophilia is a X linked coagulation disorder affecting 1 in 10,000 worldwide, with Hemophilia A or Factor VIII deficiency comprising 80% and Hemophilia B or Factor IX deficiency comprising 20% of the remaining.^{1,2} In 30% of the patients there is absence of family history, among them 80% of mothers are carriers of de novo mutations.³

Hemophilia clinically presents as bleeding into joints, muscles, soft tissues spontaneously or with mild trauma.⁴ Both factor VIII & IX deficiency cannot be differentiated clinically, but depending upon factor levels they have been classified as Mild (>5-30), Moderate (1-5) and severe (<1%) factor levels.³

In our country haemophilia patients have limited access to treatment, if accessible it is expensive.⁵ So use of blood, blood products as cheaper alternative to factor concentrate at present⁶, with risk of transfusion transmitted infections.⁷ As there is improvement in treatment of haemophilia we are facing development of inhibitors that neutralise clotting factors.⁸

Since there are varied presentations of haemophilia to emergency department and paucity of data about the same and its management made us to study various emergencies in PWH and their management.

MATERIAL AND METHODS

Case records of admitted patients with hemophilia to our emergency department of Nizams Institute of Medical sciences

hospital which is a multispeciality, tertiary care referral hospital were collected over a period of one year.

Inclusion criteria

All patients diagnosed as factor VIII or factor IX deficiency with bleeding presenting to emergency department were included.

Exclusion criteria

Bleeding from other causes like thrombocytopenia, DIC, other coagulopathies were excluded.

Information from case sheets of all patients recruited for analysis were reviewed. In the history, demographic details, symptoms with the duration, history of trauma, family history, old records of factor levels, weight and, including type of bleeding emergency were noted.

Clinical findings specifically noted were presence of. Joint bleeds, wound bleeds, and other clinical signs if present were recorded.

The investigation reports of Hemogram, chest radiograph, Factor levels, ultrasonography (carried with MYLAB60 model, eSaote company from Ahmedabad) of the part done like Abdomen, or High resolution ultrasound of the joint or Abdomen for quantifying the bleed, where ever done were noted. Contrast Enhanced Computed Tomography (CECT) of abdomen and Brain, (carried with Philips Brilliance 16 model, 16 slice CT, PHILIPS company from Netherlands) other parts done were also noted. Human Immune deficiency virus (HIV) ELISA, Hepatitis B virus (HBV), Hepatitis C virus (HCV) serology screening, Inhibitor screening were ever done were also noted.

The treatment details like medical management were noted. Tranxemic acid, Fresh frozen plasma, cryoprecipitate, factor concentrates, packed red cell transfusion and bypassing agents (Novo seven) were ever given according to the availability and treatment plan were noted and, their dose and duration were also noted.

The above data from all patients was tabulated and analyzed retrospectively. The study was retrospective audit with no patient direct identifiers, hence consent was not taken. Hospital ethics committee was informed of the study.

STATISTICAL ANALYSIS

Microsoft office 2007 was used for the statistical analysis. Descriptive statistics like mean and percentages were used to

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interpret the data.

RESULTS

Total 66 number of PWH came with emergencies. Age varied from 7 years to 57 years with mean age of 23.95 years. Mean Body weight of 48.10 kg.

Hemophilia A was present in 58 and 8 had Hemophilia B. Among 66 patients 6 had Mild, 27 had Moderate and 33 had Severe Hemophilia.

Most common presentation was Acute Hemophilic Arthropathy in 22 (33%) patients (Table-1), followed by Acute intramuscular Hematoma in 21 (31.8%), Intracranial bleed in 6 (9%), Acute Gastrointestinal (GI) bleed in 8 (12%), (upper GI 5, Lower GI 3), Hemoperitonium in 2 (3%), Hematuria in 2 (3%), Bleeding wounds in 6 (9%), Hemptysis in 1 (1.5%) (table-1).

Precipitating factors were Injury in 14, Infections in 2, seizures in 1, tooth extraction in 1, fever in 1, Boil in 1, and spontaneously in 44.

All patients under went Hemogram, coagulation studies relevant ultrasound of the affected area, where ever needed CT Scan brain, High Resolution ultrasound of the site for quantifying the bleed.

Total 42 patients were screend for HIV, HBV, HCV infection. only one patient was found to have HCV positive. 24 patients were not screened.

Since many patients were poor and as per the availblity of the components the factors were replaced in minimum required

doses. From the type of bleeding episodes Acute Arthropathy was managed with average total dose of 50 U/kg, Acute Intra Muscular hematoma with 80U/kg, Acute Gastrointestinal bleed with 120U /kg, Bleeding wounds with 120U/ kg, Intracranial bleed with 440U/kg, Hemoperitonium with 40U/kg, Bleeding gums with 30 U/kg, Hematuria with 100U/kg, Hemptysis with 20U/kg, there were no surgeries performed.

Screening for inhibitors was done in in 11patients, 3 had inhibitors, and 2 were managed with Bypassing agents recombinant factor VII (NovoSeven) 2mg. And 1 patient managed with higher doses of factor VIII.

DISCUSSION

Haemophilia is a common bleeding disorder with Haemophilia A is higher than Haemophilia B 80% to 20%⁹⁻¹⁴, in our study Haemophilia A was 87.8% to 11.2%. Of Hemophilia B, Hemophilia A was slightly higher than but similar to Jodhpur Vikas Payal¹⁴ of 91% (Table-2). Depending on the factor levels Haemophilia was divided into mild, moderate, severe. Severe Haemophilia was more common 50% followed by moderate 41%, mild 9% similar to other studies had ranging from 43 to 55.7¹³⁻¹⁸, but in Bangladesh study mild variety was more common.^{9,10,14}

Most common presentation was Acute Haemophilia arthropathy 33% which is similar toother studies^{9,10,14,17,19}, but they had hemarthrosis ranging from 82-100% but Stephenson et al²⁰ had

Sr No	Clinical presentation	Numbers %
1	Acute Hemophilic Arthropathy	22 (33%)
2	Acute Intramuscular Hematoma	21 (31%)
3	Acute Gastrintestinal Bleed	8 (12%)
4	Intracranial bleed	6 (9%)
5	Hemoperitonium	2 (3%)
6	Hematuria	2 (3%)
7	Bleeding wounds	6 (9%)
8	Hemptysis	1 (1.5%)

Table-1: Showing clinical features



Figure-1: Photograph showing (Arrows) right knee haemarthrosis

	W Schram et al	Payal et al ¹⁴	Present study
Year of study	1996 to 1998	2015	2015
Duration of the study	2years	1 year	1year
Place of study	Europe	India	India
Total patients Numbers	1005	56	66
Age in years	NA	6.85	23.95
Hemophilia Mild	-	19.64%	9.10%
Moderate	16.4%	36%	40.90%
Severe	83.6%	44.64%	50%
Presentation Arthropathy.	71.6%	73%	33%
Muscular Hematoma	NA	NA	31.8%
Gastrintestinal Bleed	NA	NA	12%
Intracranial Bleed	NA	NA	9%
Bleeding wounds	NA	NA	9%
Hemoperitonium	NA	NA	3%
Hematuria	NA	NA	3%
Transmitted Infections	HIV 32.3% HBV 73.9% HCV 91.6%	HIV NIL HBV NIL HCV NIL	HIV NIL HBV NIL HCV 1.5%
Inhibitors	8.3%	NA	4.5%

Table-2: Showing comparing present study with other studies

65%. Among arthropathy knee (Figure-1) was most commonly involved in about 55% followed by ankle in 30% and elbow in 10%^{10,14,21} HL Minhas²² also reported knee joint as common joint involved followed by elbow and ankle.^{10,14,21} In Bangladesh study^{13,23} Stephenson et al²⁰, Aronstantan et al²⁴ reported ankle joint was commonly involved followed by elbow.

Next common bleeding manifestation was intramuscular Hematoma in 31.8% which was similar to Stephenson et al²⁰ and Alcalays.²⁵

Among muscular Hematoma Ileoasoas bleed was seen in 10% of the patients. Similarly reported by C.Balkan et al²⁶ 7 and femoral neuropathy was seen in all but 1 patient, which is less than seen with C.Balkan et al²⁶, K.Ghouse et al²⁷ who reported by 57%. All ileopsoas bleed were diagnosed by ultrasonography which is similarly reported by (Balkan et al.^{2,4,8,26} Ultrasonography is cheap and faster and reliable. K. Ghouse et al²⁷ reported 0.5% incidence of femoral neuropathy and Saraf. L singh 2003 et al²⁸ reported incidence of 15%. We observed joints and muscle bleeds in 64% of our patients which is similar to Stephenson et al.²⁰

In our study Intra cranial bleed was seen in 6% similar to Traivaree et al²⁹ 6%, Ghouse et al 7%³⁰, but Revel-Vilk et al³¹ reported 10-5% and Stiefles et al³², reported 36.6% of ICH. We noted Acute GI bleed in 12% (Upper GI 8%, Lower GI 4%) which is less than Forbes et al³³ who reported 25%.

Other presentation in our study were Hemoperitonium in 3%, Hematuria in 3%, Bleeding wounds in 9%, Hemoptysis in 1.5%. Most common precipitating factor was injury in 21.2% the patients. Similarly reported by HL Minhas²² group. In 66% of the patients there was no precipitating cause i.e., there was spontaneous bleed.

Since many patients were poor, as per the availability of components the factor were replaced in minimum required doses. Acute Arthropathy was managed with around Average total dose of 50 U/Kg (10%) which is similar to the WFH guidelines³⁴ and also same was recommended by A Srivatsava et al³⁵, but south african and stephenson et al²⁰ use slightly higher dose of more than 50 U/Kg. while treating Intra muscular Hematoma total around 80 U/Kg factor was given which is similar to A.Srivastava et al³⁵, and WFH guidelines Ileo psoas bleed was also treated with around 80 U/Kg which is similar A.Srivastava³⁵ and WFH guideline.³⁴ But Balkan et al²⁶ used > 100 U/Kg.

Intra cranial bleed was treated with 440 U/Kg which is similar to WFH guidelines³⁴ but Rolt C.R.Ling³⁶ used higher dose. K.Ghouse et²⁷ also used low dose. And Acute GI bleed was treated with 120 U/Kg which is similar to WFH guideline³⁴ but less than P-A Kouides et al.³⁷

Bleeding gums were managed with 30 other Hemoperitonium (40 U/Kg), Hematuria 100 U/Kg, Hemoptysis 20 U/Kg which is similar to doses recommended by Alok srivatsava³⁴ guidelines as well as M.Chandy.³⁸

Inhibitors were seen in 3 patients (4.5%). Among them (15%) were responders to high dose of factor (high responders)^{39,40} R.Ghouse C.²⁷ reported haemophilia incidence of 8.2% Sharition et al^{40,41} reported 14% inhibitors and 3% were high responder.²⁶ E Sughip et al^{41,42} reported 28% having inhibitor and 4% were high responders. Also Beyer et al^{42,43} used high doses in high dose responders.

2 Patients of inhibitors were treated with recombinant factor VII

a total dose of 2mg was given, all responded to the treatment. Similar low doses were used by Beyer et al.⁴² But high doses of 200micro gm /kg were used by Parameswaram et al.⁴³

A total of 42 patients was screened for transmitted infection only. One patients 2% was found to have HCV positive, which is less than Iranian study reported (15.6% to 76.7%, Allavian et al)^{44,45}, in India (2008-2009) 7.5% by Mittal et al.^{7,31-33} HCV patient was treated with peginterferon and ribavarin. In our study no patients had HIV & HBV infection, which is similar to (Payal et).¹⁴

CONCLUSION

Hemophilia emergencies are common, in resource poor settings minimal factor replacement can stop bleeding and improve the outcome.

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