ORIGINAL RESEARCH PAPER

Medical Science

THE CORRELATION BETWEEN CLINICAL AND HEMATOLOGICAL PARAMETERS IN HAEMOPHILIA IN A TERTIARY CARE HOSPITAL

KEY WORDS: Hemophilia, Factor assay, Factor VIII, Factor IX

Dr Seetharam Anandram Assistant Professor, Hematology Unit, St. John's Medical College, Bangalore, Karnataka

Dr Aaron Charles Lobo Senior Resident, Hematology Unit, St. John's Medical College, Bangalore, Karnataka

Dr Cecil Reuben Ross Professor & HOD, Hematology Unit, St. John's Medical College, Bangalore, Karnataka

Dr Maneesh Sulya* Associate (Designated) Professor Pathology, Gandhi Medical College, Bhopal, M.P. *Corresponding Author

ABSTRACT

Introduction: Haemophilia is the most common inherited coagulation disorder with X-linked recessive inheritance. The males are usually affected while females are often carriers of the disease. Haemophilia is caused by the deficiency of coagulation factor VIII (haemophilia A) or factor IX (haemophilia B) resulting from mutations of the clotting factor gene. This study looks at the clinical manifestations and laboratory features of patients with haemophilia.

Methods: This retrospective study was carried out at the Department of Medicine in the Hematology Unit, for a period of 1-year from July 2018 to June 2019. The patient's demographics, history, age, clinical features were studied in detail. Complete haemogram, coagulation tests including PT, APTT, mixing studies and factor assays were documented.

Results: Out of 119 cases, 108 cases were of haemophilia A while 11 cases were of haemophilia B. All the cases were males. The predominant presenting symptom was hemarthrosis followed by post-traumatic bleeding. The knee joint was most commonly involved, followed by ankle, elbow and shoulder joint. 66.38% of cases had severe factor deficiency, 17.64% moderate and 15.96% mild deficiency.

Conclusion: A diagnosis of haemophilia was commonly suspected based on prolonged APTT in a bleeding patient or picked up incidentally. The factor assay helped to confirm the diagnosis. The severity of the disease correlates with the frequency and the severity of the bleed.

INTRODUCTION

The word haemophilias derives its genesis from the Greek word *haima*, meaning blood and *philia* meaning love.[1] Haemophilia is a rare disorder. The incidence is 1in 10,000 births (or 1 in 5,000 male births) for haemophilia A and 1 in 50,000 births for haemophilia B.[2] Haemophilia usually occurs in males, whereas females are generally carriers.[3] This is an X-linked recessive disorder characterized by the deficiency of clotting factor VIII (FVIII) or factor IX(FIX).[4] It is the most common congenital bleeding encountered in clinical practice affecting men. Inadequate FVIII levels result in the insufficient formation of the intrinsic tenase complex (FIXa, FVIIIa, Ca2+ and Phospholipids) which subsequently leads to reduced generation of thrombin with impaired fibrin deposition and clot formation[4].

The world federation of haemophilia classifies the severity of the disease based on the level of clotting factors (Table no 1)

Level	% of normal factor activity in blood	Number of international Unit(IU) per milliliter of whole blood
Normal range	50%-150%	0.50-1.5IU
Mild hemophilia	5%-<40%	0.05-0.40IU
Moderate hemophilia	1%-5%	0.01-0.05IU
Severe hemophilia	Less than 1%	Less than 0.01IU

The patients with severe haemophilia usually bleed frequently into their muscles or joints. The frequency of bleed may be as frequent as one to two times per week. Bleeding is often spontaneous. The patients with moderate haemophilia bleed less frequently, usually not more than once a month. They may suffer bleed for a prolonged bleed after surgery, a bad injury, or dental work. A person with moderate haemophilia will rarely experience spontaneous bleeding. The patients with mild haemophilia usually bleed as a result of major surgery or injury. They do not bleed often, and some may never have a bleeding problem. [5] The replacement of the deficient factor is the mainstay of treatment, however, when the factor concentrates are not available usually due to lack of affordability, options used includes transfusion of whole blood, FFP (fresh frozen plasma) and Cryoprecipitate and use of antifibrinolytic agents. [6]

The aim of this study was to

1. Assess the severity of the condition in our patient cohort.
2. Correlate the severity with the clinical manifestation i.e. bleeds.
3. Assess the effectiveness of the treatment

MATERIALS AND METHODS

This retrospective study was conducted on haemophilia patients admitted or presenting with bleeding between July 2018 and June 2019 to St John's Medical College Hospital.

A detailed clinical history was obtained from the accompanying parent/guardian with particular emphasis on the following parameters: demographic features, duration of symptoms, symptom profile, family history, and the number of previous bleeds and factor infusion or blood product transfusion.

The diagnosis was confirmed using clinical records and factor assays.

A detailed clinical examination was done with particular emphasis on joints examination. Appropriate factors were given based on the diagnosis. The dose of factor VIII/IX was calculated based on the severity. Mild, moderate, and severe haemophilia were defined as those having a factor level of >5-<40%, 1-5%, and <1% respectively.

RESULTS

The study was conducted over one year between July 2018 to

June 2019. A total of 119 patients(Haemophilia A- 108; haemophilia B-11) were studied. The age range of these patients varied from 1 year to 90 years. (**Table 02**) . The majority of the cases (n = 56, 47.05%) were in the age group of 01-20 years, followed by 40 cases (33.61%) in the age group of 20.1-40 years, 21 patients(17.64%), 40.1-60 years and 4 patients(3.36%) above 60 years.

In our study, the most common presentation was hemarthrosis, followed by muscle and subcutaneous hematoma, dental bleed, post-traumatic bleed, epistaxis and injection hematoma. (**Table 03**)

The knee joint was the predominant joint affected (68.06 %) followed by ankle joint (17.64%), elbow (10.80%), hip(3.36%) and shoulder joint(0.84%). The activated partial thromboplastin time was prolonged in all cases.

Factor assay done showed 79(66.38%) patients had severe factor VIII deficiency(both haemophilia A& B combined), 21 (17.64%) patients had a moderate deficiency, and 19(15.96%) patients had mild deficiency **(Table 03)**

Table 2-The presentation of haemophilia according to age

Age	Total	
	Number(119)	Percentage (%)
0-20 years	56	47.05
20.1-40 years	40	33.61
40.1-60 years	21	17.64
>60 years	04	03.36

Table 3- Distribution of factor level and severity of patients with hemophilia

Severity and Factor level	Total	
	Number (119)	Percentage(%)
Mild (5-<40%)	19	15.96
Moderate (1-5%)	21	17.64
Severe (Less than 1%)	79	66.38

Discussion

Haemophilia is the most common inherited bleeding disorder presenting to our centre, in keeping with prevalence worldwide.

We had patients right from 3 months of age to 90 years. The presence of older-aged individuals is the reflection of the significant improvement in the care and management of these patients. This is mainly due to better availability of factors and increasing awareness of the condition among public and health care professionals.

All our patients were males in keeping with the mode of inheritance of this condition. (7)

The knee joint was the predominant joint affected by haemarthrosis followed by ankle, elbow and shoulder. Our findings were similar to other studies done by Nikethan et al., Agarwal et al. and Srivastava et al. (7,9,10)

APTT was prolonged in all our patients with an average value of 73.3 sec in our study. This value was similar to studies done by Dube et al. and Craig S. Kitchens. and Nikethan et al. (7,12,13)

In our study, the percentage of mild, moderate and severe disease where 15.9%, 17.6%,66.4% which is similar to studies done by Srivastava et al., Shathala Devi et al. and Nikethan et al. (10,11,7) (Table 4)

Table 4 :Comparison study between factor level and severity in hemophilia

Severity & factor level	Alok Srivastava	Shanthala Devi	Nikethan B.et	Present (%)
Mild (5-<40%)	15%	12%	11%	15.96
Moderate (1-5%)	15%	14%	22%	17.64
Severe(< 1%)	69%	74%	67%	66.38

CONCLUSION

Haemophilia A is more common than B. The most commonly involved joint is Knee followed by ankle, elbow and shoulder. The demographic distribution of our patients was similar to other studies done in India. Our study also indicates significant improvement in delivery of care in haemophilia patients.

ACKNOWLEDGEMENT

I am immensely thankful to Dr Cecil Ross, Professor and HOD Haematology Unit, Internal Medicine, Dr.Sitalaxmi A, Professor and HOD TM&IH, Dr Vandana Bharadwaj, Associate Professor and HOD, Pediatrics Haemato-Oncology and Dr Seetharam A, Assistant Professor, who have thought me and motivated me.

Funding: No funding sources

Conflicts of interest: None declared

Ethical approved: Approved by Hemophilia Society in Bangalore Chapter, St. John's Medical College, Bangalore.

REFERENCES

1. Douglas Harper. "Online Etymology Dictionary". Archived from the original on 6 March 2008. Retrieved 10 October 2007.
2. World Federation of Hemophilia Frequently Asked Questions About Hemophilia Archived 2008-06-12 at the Wayback Machine
3. "U.S. National Library of Medicine". Archived from the original on 12 October 2007. Retrieved 2 December 2007.
4. Kabel AM. Bleeding disorders: insights into aetiology, pathogenesis, diagnosis and management. Int J Hematol Disord 2014;1:22–6. doi: https://doi.org/ 10.12691/ijhd-1-1-4.
5. World Federation of Hemophilia improves the severity of hemophilia (Updated May 2012)
6. Marwaha N. Transfusion related complication in hemophilia. Asian J Transfus Sci 2013;7:6-7
7. Nikethan B.et al: A clinico-hematological profile of hemophilia-at a tertiary care centre. IJBMS 2015: Vol.-5, Issue- 1, P. 511-515
8. Bick R, Vascular thrombohemorrhagic disorders, Hereditory and Acquired, Clinical Application. J. thrombo hemost: 2001;7(3): 178-94.
9. Agarwal MB, Mehta BC, Bhanotra PC. Classical hemophilia. J Assoc Physicians India. 1981;29:385-389.
10. Srivastava A. editor. In : Guidelines for management of hemophilia in India. New Delhi. Hemophilia Federation 2003;p.7-9.
11. Shanthala Devi AM, Sitalakshmi S, Srikrishna A, Damodar P, Mathew T, Ernest JP. Profile of inherited bleeding disorder in a teaching hospital. Indian J Hematol & Blood Transf 1999;17:16-18.
12. Dube B, et al. Hemophilia and Christmas disease –a clinical and hematological study. J Assoc Physicians. India. 1972;20:47-54
13. Criag S. Kitchens. Occult hemophilia. John Hopkins Med J, 1980;147:255-259.