ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Annual Bleeding Rate In Hemophilia Children Without Inhibitors Attending Tertiary Care.

R Ramanathan[1]*, and EJ Divya[2].

[1]Professor & HOD, Department of Paediatrics, Government Medical college and Hospital Cuddalore District, Tamil Nadu, India.
[2]Post Graduate, Government Medical College and Hospital Cuddalore District, Tamil Nadu, India.

ABSTRACT

Hemophilia is a X- linked rare bleeding disorder characterised by deficiency of factor 8 (hemophilia A), Or deficiency of factor 9 (hemophilia B), which is further leads to spontaneous bleeding manifestation in the affected individuals for which factor replacement therapy is given to reduce the bleeding manifestation .Annual bleeding rate measure the no of bleeding episodes in the haemophilia children and is somewhat related to the inhibitors present in the body. This is a observational study conducted among the haemophilia children under 18 years attending the Government Medical college & hospital Cuddalore District as OPD/IP care . Annual bleeding rate was observed in those without inhibitors. Out of 33 children, 25 children belonged to Hemophilia A and 6 children had Hemophila B , 2 children presented with both Hemophilia A & Von willibrand deficiency; 2 out of 33 children had inhibitors. The annual bleeding rate among the 31 candidates was less than 5 bleeding per year in 51.6% , 32 % had annual bleeding rate between 5- 10 times/ year ,16% had bleeding greater than 10 episodes per year.Annual bleeding rate is a important factor in recognising the need for factor replacement therapy given as on demand or prophylactic .Ideally it is crucial in starting with prophylactic which aids in reducing the annual bleeding rate in children halting the disease progression to end stage disability.

Keywords: Hemophilia, Annual bleeding Rate, Inhibitors.

https://doi.org/10.33887/rjpbcs/2025.16.5.23

*Corresponding author

ISSN: 0975-8585

INTRODUCTION

Hemophilia, often referred to as the "Royal disease," is a rare inherited bleeding disorder that follows an X-linked recessive inheritance pattern. Hemophilia A results from a deficiency in coagulation factor VIII, while deficits in factors IX and XI cause Hemophilia B and C, respectively. According to the World Federation of Hemophilia's 2018 global report, over 200,000 individuals were identified with Hemophilia worldwide, with approximately 82.5% (173,711) diagnosed with Hemophilia A and around 16% (34,289) with Hemophilia B [2]. In India, The Hemophilia Federation of India, operating through 87 local chapters and 75 treatment centres (complete and partial), has recorded about 21,800 cases—substantially fewer than the estimated national burden of nearly 70,000.

In Hemophilia patients plasma does not contain clotting factors in sufficient amount required for coagulation in case of injury or breech in blood vessel .In case of injury the clot formed by platelet plug is not stable and cannot maintain haemostasis thus the patient bleeds for a long duration than a normal individual it may last days to weeks in case of severe deficiency .Bleeding into closed spaces such as joint spaces, intramuscular compartments , intracranial space is fatal if not treated timely. Diagnosis requires clinical vigilance and appropriate laboratory investigations, particularly in children presenting with unexplained bleeding. Management focuses around the use of clotting factor concentrates (CFCs), which are expensive and complicated by the potential development of inhibitors.

The disease significantly impacts the patient's lifestyle and imposes considerable psychological and financial strain on families. Preventive (prophylactic) treatment has been shown to reduce the frequency of bleeding episodes and mitigate severe complications such as intracranial haemorrhage and joint disease (arthropathy).

MATERIALS AND METHODS

This is a observational study conducted among 33 patients attending as outpatient or inpatient in Government Medical College& Hospital –Cuddalore District over a period of 1 year from December 2023 to December 2024.

Inclusion Criteria

- All haemophilia patients (A&B) aged between 0- 18 years willing to participate in the study .

Exclusion Criteria

- Hemophilia children who have positive inhibitors
- Aged more than 18 years
- Hemophilia children not willing to participate.

Data was collected by the principle investigator with a predesigned semi structured questionnaire .A thorough clinical history was taken including most common bleeding manifestation, history of previous blood transfusion, treatment done, age at first presentation, age at confirmed diagnosis, development of inhibitors, frequency of replacement therapy given, history of bleeding following vaccination, All these patients were then subjected to meticulous clinical examination and relevant blood investigations were taken Blood investigations include – complete blood count to rule out platelet disorders ; Coagulation profile , factor assay , inhibitor assay .

RESULTS

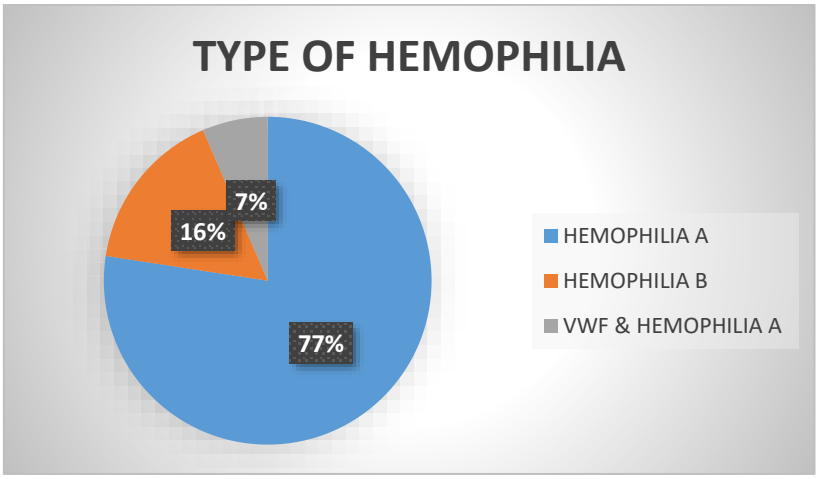
The data was analysed using arithmetic mean, 33 participants were studied, 2 participants were excluded from the study since they were having inhibitors and
the results are tabulated as follows.

ISSN: 0975-8585

Table 1: Type Of Hemophilia Among Participants

TYPE OF HEMOPHILIA	NO OF PARTICIPANTS
HEMOPHILIA A	24
HEMOPHILIA B	5
VWF & HEMOPHILIA A	2
TOTAL	31

Chart 1: Type Of Hemophilia In Participants

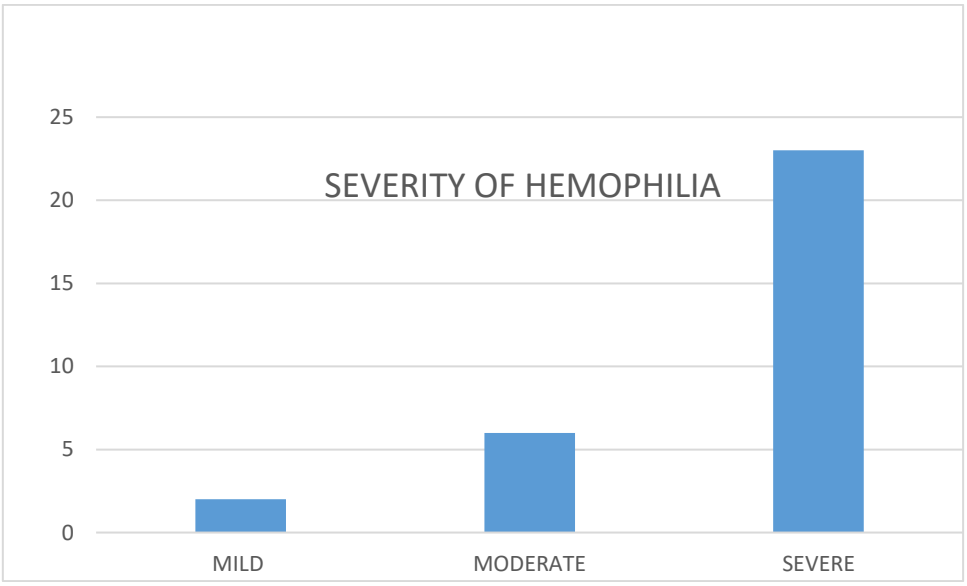


Among 31 hemophilia children 77% of children had haemophilia A and 16 % had haemophilia B and 7% of children had both von willibrand and haemophilia A together.

Table 2: Severity Of Hemophilia Children

SEVERITY OF HEMOPHILIA	FREQUENCY(n)
MILD	2
MODERATE	6
SEVERE	23
TOTAL	31

Chart 2

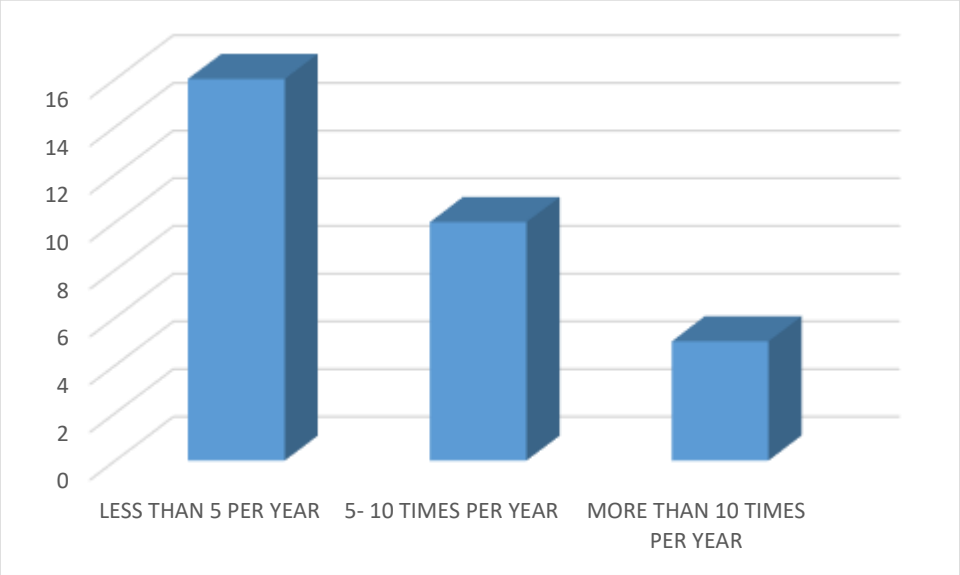


Among 31 participants majority of the children had severe haemophilia with factor levels less than 1 %, 19 %(6) of children belongs to the moderate haemophilia with a factor level of 1-5 %, and only 6% have a mild variant of haemophilia. This emphasis that mild and moderate variant are seldom diagnosed as they have near normal situation with rare bleeding manifestation especially prolonged bleeding following trauma or during surgical procedures. The severe variant haemophilia requires frequent factor replacement which predisposes to inhibitor formation.

Table 3: Annual Bleeding Rate In Hemophilia Children

ANNUAL BLEEDING RATE	FREQUENCY
LESS THAN 5 PER YEAR	16
5- 10 TIMES PER YEAR	10
MORE THAN 10 TIMES PER YEAR	5
TOTAL	31

Graph 3: Annual Bleeding Rate In Hemophilia Children



Annual bleeding rates of less than 5 per year was present in 51% of children , 31% had bleeding rates between 5- 10 times / year . A higher rate of greater than 10 bleeds per year was in 16% of children necessitating frequent factor replacement and they would be the appropriate candiadate for using extended half life products , bypassing agents .

DISCUSSION

In this study the most common type of Hemophilia observed was Hemophilia A- (77%) as compared to Hemophilia B (16 %). No patient with Hemophilia C was observed in our studied. One Male & Female child was identified to have both Hemophilia A and type 3 VWF deficiency. This is similar to study done Mohd Razaq et al where haemophilia patients with A corresponds to higher percent as 81%, and 18.4% belongs to type B. However there is contrast to study done by Khan F et al , Mehta et al whereby the percent of haemophilia A is higher 88.3%& 91% respectively [3-15]

Regarding severity majority of the our cases belonged to severe range of Hemophilia A & B with 77.4 %, the rest of the participants belonged to moderate range . This is synchronous with the studies done by other parts of India where the more no of cases fall into the severe category. Study done by Venkata Vijayalakshmi vankatu et al has 62.5 % of children belonging to severe haemophilia , Mehta et al has even higher prevalence of 80% of children belonging to severe haemophilia .This trend highlights that severe Hemophilia will have more bleeding manifestation and will result in hospitalisation with increased factor usage [13, 15].

Annual bleeding rate is important factor in recognising the need for factor 8/9 transfusion as on demand or in prophylactic group .Ideally it is crucial in starting of with prophylactic factor replacement which aids in reducing the annual bleeding rate in children halting the disease progression to end stage disability .Our study represents 51% were having less than 5 bleeding manifestation per year which is similar to a study done by patel et al which has 46.42% with bleeding less than 5 per year . In contrast study done by Sahoo T et al in a tertiary care in Uttar Pradesh was around 68% meaning there is better prognosis of disease progression [14]. Greater development of inhibitor is potential to children who has greater than 10 bleeds per year however the percentage was less 16% in our study which was similar to study done by Patel et al and Mehta et al corresponding to 5%& 11% respectively.

CONCLUSION

Hemophilia is the most underrated bleeding disorder when compared with disease like sickle cell anaemia/thalassemia. The recent advances in innovative drugs like Emicizumab, fitusuran gives a hope of better life with less hospitalisation in these patients who can lead a near normal life. However, there is long road to be traversed to reach the final destination of a near normalcy in these children with adequate support from local government, Hemophilia federation and other support help groups

Limitation

This is an observational study done at a tertiary hospital, the incidence of the Hemophilia and the incidence of inhibitors in patients receiving the factor replacements could not be studied.

REFERENCES

[1] Mannucci PM, Tuddenham EG. The Hemophilias—from royal genes to gene therapy. N Engl J Med. 2001;344(23):1773–1779.
[2] World Federation of Hemophilia. Annual Global Survey 2018. Montreal: WFH; 2019.
[3] Hemophilia Federation of India. Available from: https://www.Hemophilia.in [Accessed June 2025].
[4] Srivastava A, Brewer AK, Mauser-Bunschoten EP, et al. Guidelines for the management of Hemophilia. Hemophilia. 2013;19(1):e1–47.
[5] Iyer V, Madkaikar M. The challenge of Hemophilia care in India. Indian J Pediatr. 2019;86(6):521–526.
[6] Mital M, Shah R, Bhatnagar N. Diagnostic delay in rural Hemophilia patients: a persistent challenge. J Pediatr Hematol Oncol. 2020;42(4):e255–e258.
[7] Saxena R, Pati HP. Public health neglect of Hemophilia in India. Indian J Med Res. 2016;144(6):721–723.
[8] Peyvandi F, Garagiola I, Young G. The evolving landscape of Hemophilia care. Lancet. 2016;388(10040):187–197. 9. Blanchette VS, Key NS, Ljung LR, et al. Subcutaneous emicizumab in pediatric Hemophilia A: a global experience. N Engl J Med. 2019;379(4):329–337.
[9] Mahlangu J, Oldenburg J, Paz-Priel I, et al. Emicizumab prophylaxis in non-inhibitor Hemophilia A patients. N Engl J Med. 2018;379(9):811–822. 7311. [Author(s)].
[10] Srivastava A. Preventing complications in pediatric Hemophilia: a call for prophylaxis. Indian Pediatr. 2017;54(2):96–97.
[11] Tuddenham EGD. The Royal Disease. In: Hemophilia A and B: Molecular Insights. London: Springer; 2008. p. 3–10.
[12] Vantaku VV, Padma KJ, Mohan M, Manikyamba D. Clinical profile of Hemophilia children admitted in a tertiary care hospital in South India: a cross 76sectional study. Int J Contemp Pediatr. 2024;11(2):233–238 doi:10.18203/2349-3291.ijcp20233233.
[13] Sahoo T, Naseem S, Ahluwalia J, Marwaha RK, Trehan A, Bansal D. Hemophilia in children: a clinico-epidemiological profile from Western Uttar Pradesh. Pediatr Rev Int J Pediatr Res. 2022;9(5):215–221.
[14] Khan MJA, Hafeez A, Butt QR, et al. Clinicopathological parameters and quality-of-life assessment in adult and pediatric Hemophilia patients at a tertiary care centre. Haemoph Off J WF Hemophil. 2023;29(1):8–17.
[15] Mehta R, Singh P. Clinical presentation of pediatric Hemophilia at Jodhpur: a cross-sectional study. J Hematol Pract. 2022;18(3):210–217.