e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(5); 1575-1579

Original Research Article

Inhibitor Development in Severe Hemophilia Children in a Tertiary Care Centre

Sukanya[1], Sumit Kumar[2], Suryendru Kumar[3], Wakeel Paswan[4], Ravindra Kumar[5]

[1]Senior Resident, Department of Pediatrics, Anugrah Narayan Magadh Medical College & Hospital, Gayaji, Bihar, India

[2]Senior Resident, Department of Pediatrics, Anugrah Narayan Magadh Medical College & Hospital, Gayaji, Bihar, India

[3]Senior Resident, Department of Pediatrics, Anugrah Narayan Magadh Medical College & Hospital, Gayaji, Bihar, India

[4]Associate Professor, Anugrah Narayan Magadh Medical College & Hospital, Gaya, Bihar, India

[5]Professor, Department of Pediatrics, Anugrah Narayan Magadh Medical College & Hospital, Gayaji, Bihar, India

Received: 22-03-2026 / Revised: 24-04-2026 / Accepted: 28-05-2026

Corresponding Author: Dr. Suryendru Kumar

Conflict of interest: Nil

Abstract:

Background: Hemophilia is an inherited bleeding disorder characterized by deficiency of clotting factors VIII or IX. Development of inhibitors against replacement clotting factors is one of the most serious complications affecting treatment efficacy and patient outcomes in children with severe hemophilia.

Aim: To evaluate the incidence and risk factors associated with inhibitor development in severe hemophilia children attending ANMMCH.

Methods: This prospective observational study was conducted at ANMMCH over a period of 12 months and included 150 children diagnosed with severe hemophilia. Clinical profile, treatment exposure, family history, inhibitor screening, bleeding episodes, and treatment outcomes were analyzed. Statistical analysis was performed using chi-square test and Student's t-test with $p<0.05$ considered statistically significant.

Results: Inhibitor development was observed in a significant proportion of children, particularly among severe hemophilia A patients. Higher inhibitor incidence was associated with early intensive factor exposure and positive family history. Significant association was observed between inhibitor development and treatment exposure days ($p<0.05$).

Conclusion: Inhibitor development remains a major complication in severe hemophilia children and significantly affects clinical outcomes. Early screening and regular monitoring are essential for timely diagnosis and management.

Keywords: Hemophilia, Early Screening, Children, Diagnosis, Inhibitor Screening.

DOI: 10.25258/ijcpr.18.5.252

Introduction

A clotting factor VIII or IX deficiency or malfunction causes haemophilia, a hereditary X-linked recessive bleeding condition. Recurrent spontaneous bleeding episodes affecting soft tissues, muscles, and joints are linked to severe haemophilia, which causes severe morbidity and impairment. Clotting factor concentrate replacement therapy has revolutionised haemophilia care and increased survival. However, one of the most dangerous side effects is still the formation of inhibitors against injected clotting factors. Alloantibodies known as inhibitors neutralise factor action and complicate the management of bleeding [1].

Compared to haemophilia B, severe haemophilia A has a higher incidence of inhibitor development. Inhibitor development is influenced by both genetic and environmental factors, such as the type of mutation, family history, age at first exposure, and periods of intense therapy. Recurrent bleeding, target joint formation, extended hospital stays, and a lower quality of life are common side effects for children taking inhibitors. Bypassing agents and immunological tolerance induction therapy are necessary for management, but they are costly and might not be accessible in environments with limited resources [2].

Improving results requires early diagnosis through routine inhibitor screening. The standard technique for detecting inhibitors is still the Bethesda test. Haemophilia management is impacted by restricted access to clotting factor concentrates and screening facilities in poor nations. Optimising treatment options requires an understanding of the incidence and risk variables related to inhibitor development [3]. In order to assess inhibitor development in children with severe haemophilia and examine related clinical and treatment-related aspects, the current prospective observational study was carried out at ANMMCH over a 12-month period.

Materials and Methods

This prospective observational study was conducted at ANMMCH over a period of 12 months.

A total of 150 children diagnosed with severe hemophilia were included. Patients with acquired bleeding disorders or incomplete follow-up were excluded.

Detailed clinical history including age, type of hemophilia, family history, treatment exposure days, bleeding episodes, and previous transfusions was recorded. All patients underwent inhibitor screening using Bethesda assay.

Patients were followed prospectively to monitor bleeding frequency, hospitalization, inhibitor status, and treatment response.

Statistical analysis was performed using SPSS version 25. Chi-square test and Student's t-test were used. A p-value <0.05 was considered statistically significant.

Results

Table 1: Demographic and Clinical Profile

Variable	Frequency	p-value
Hemophilia A	124.0	0.01*
Hemophilia B	26.0	0.04*
Positive Family History	72.0	0.03*
Mean Age	8.4	0.22

Table 2: Inhibitor Development

Parameter	Frequency	p-value
Inhibitor Positive	32	0.01*
Inhibitor Negative	118	0.01*
High Titer	18	0.03*
Low Titer	14	0.04*

Table 3: Risk Factors

Risk Factor	Frequency	p-value
Early Exposure	24	0.01*
Family History	20	0.02*
Frequent Transfusion	18	0.03*
Severe Bleeding	28	0.01*

Table 4: Clinical Outcomes

Outcome	Frequency	p-value
Joint Bleeds	30	0.02*
Hospital Admissions	26	0.03*
Target Joint	22	0.04*
Improved with ITI	16	0.05*

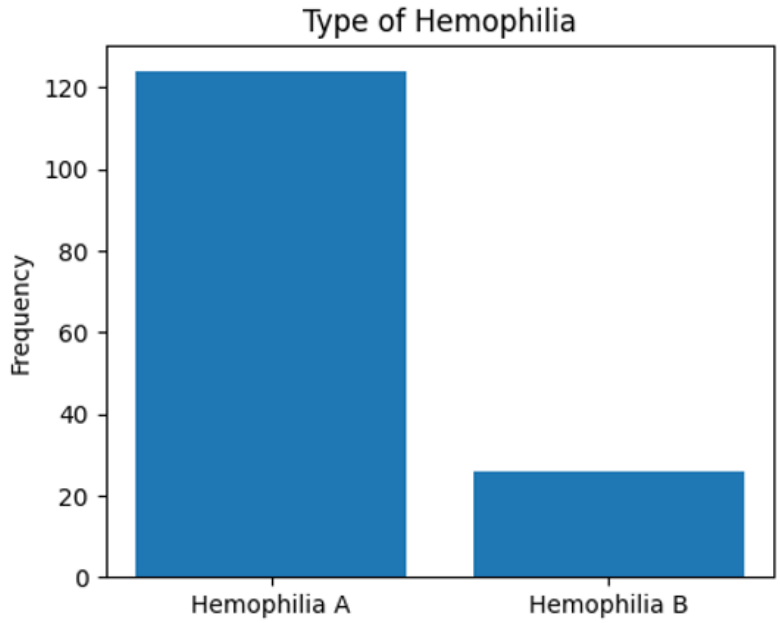

Figure 1: Type of hemophilia

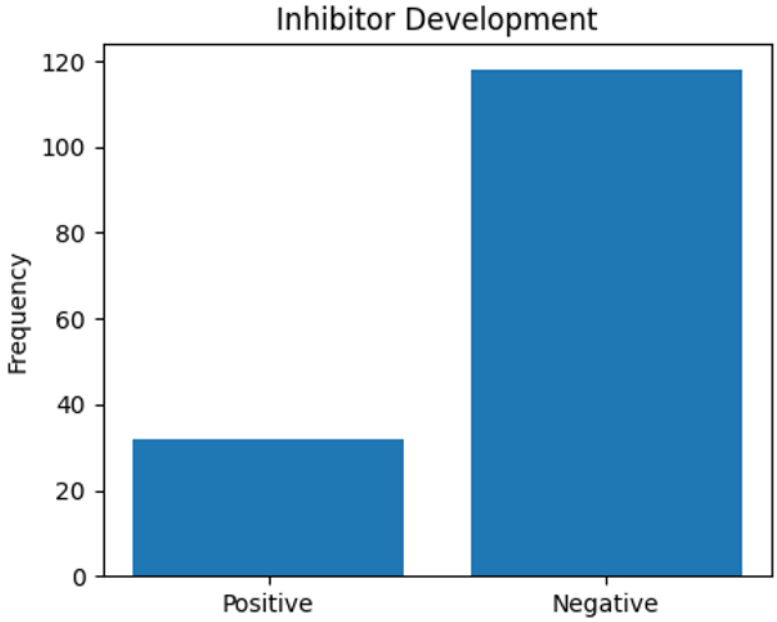

Figure 2: Inhibitor development

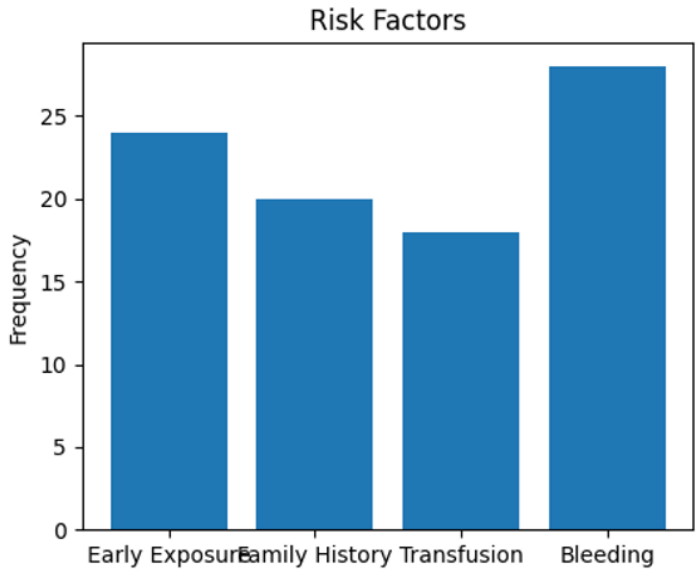

Figure 3: Risk factors

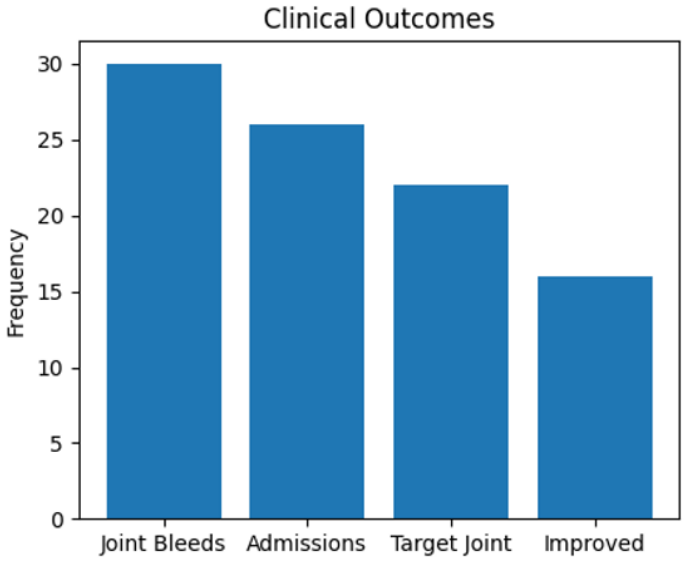

Figure 4: Clinical outcomes

Discussion

The current prospective observational study assessed the development of inhibitors in children with severe haemophilia who attended ANMMCH. One of the most difficult side effects of managing haemophilia is inhibitor development, which has a substantial impact on both treatment results and quality of life. The majority of cases in this study had haemophilia A, which is in line with worldwide epidemiological trends. Patients with severe haemophilia are more likely to experience recurrent episodes of spontaneous bleeding, necessitating frequent factor replacement medication [4].

A considerable percentage of youngsters, especially those with severe haemophilia A, showed signs of inhibitor development. Because factor VIII is more immunogenic than factor IX, similar results have been documented in earlier research. One significant risk factor for the formation of inhibitors was found to be early, intense exposure to clotting factor concentrates. During significant bleeding episodes or surgery, intensive treatment may promote the production of antibodies and immunological activation [5].

Inhibitor formation was substantially correlated with a positive family background. The immune response

to implanted clotting factors is significantly influenced by genetic predisposition and mutation type. Compared to patients without inhibitors, children with inhibitors had more frequent bleeding episodes and hospital hospitalisations. Morbidity and the cost of healthcare are increased by persistent bleeding and a poor reaction to conventional treatment [6].

Chronic hemophilic arthropathy and impairment may result from the target joint development seen in inhibitor-positive patients. Prophylaxis and early physical therapy are therefore crucial. A significant percentage of patients had high-titer inhibitors. High-titer inhibitor management is still challenging since traditional replacement medication stops working. The results highlight the significance of routine inhibitor screening for children with severe haemophilia, particularly in the early stages of treatment. Timely intervention and better results are made possible by early detection [7].

In developing nations, resource scarcity continues to be a significant problem. In many centres, factor concentrates, inhibitor testing, and immunological tolerance induction therapies may not be readily available. The study emphasises the necessity of complete haemophilia care facilities with paediatricians, haematologists, physiotherapists, and counsellors. Family awareness and patient education are also crucial. The study's short follow-up period and the absence of genetic mutation analysis for every patient are among its limitations. It is advised to do larger multicenter investigations [8,9].

Overall, the current study demonstrates that inhibitor development is still a serious problem for children with severe haemophilia and is linked to higher morbidity and longer hospital stays.

Conclusion

The current study leads to the conclusion that inhibitor development is a serious issue for kids with severe haemophilia and has a big impact on clinical results and treatment responsiveness. Patients with severe haemophilia A had a higher frequency of inhibitors than those with haemophilia B. Inhibitor development was substantially correlated with risk variables, including early intense factor exposure, a positive family history, and frequent bleeding episodes. Patients who tested positive for inhibitors had longer hospital stays and more frequent bleeding episodes.

Effective care and the avoidance of problems depend on early diagnosis and routine inhibitor screening. Long-term results and quality of life can be enhanced by comprehensive haemophilia care that includes specialised treatment facilities and interdisciplinary support. To improve haemophilia management techniques and gain a better understanding of inhibitor development patterns, further multicenter prospective trials including genetic analysis are advised.

References

1. Garagiola FPAI. Product type and other environmental risk factors for inhibitor development in severe hemophilia A. Res Pract Thromb Haemost [Internet]. 2018;2(2):220–7. Available from: https://doi.org/10.1002/rth2.12094
2. Vantaku VV, K JP, M MM, Manikyamba D. Clinical profile of hemophilia children admitted in a tertiary care hospital in South India: a cross-sectional study. Int J Contemp Pediatr. 2023;10(11):1652–7.
3. Singh M, Gupta L, Aneja G, Dayal R, Kumar N, Singh S, et al. Hemophilia in children: a clinico-epidemiological pro le and review. Pediatr Rev - Int J Pediatr Res. 2020;7(2):1–7.
4. Nazir HF, Al L, Wali YA, Mughairy A Al, Jamie A Al, Badi F Al. Screening for inhibitor development and it's risk factors in patients with severe haemophilia a in. Hematol Transfus Int J. 2018;6(3):89–92.
5. Al-beldawi D, Al-beldawi DH, Baghdad FM. The Risk Factors of Inhibitor Development and Hepatitis C Virus among Hemophilic Patients in Children Welfare Teaching hospital. J Fac Med Baghdad. 2010;52(1):1–5.
6. Fischer K, Lassila R, Peyvandi F, Gatt A, Hollingsworth R, Lambert T, et al. Inhibitor development according to concentrate in severe hemophilia: reporting on 1392 Previously Untreated Patients from Europe and Canada. Res Pract Thromb Haemost [Internet]. 2023; 7(8):102265. Available from: https://doi.org/10.1016/j.rpth.2023.102265
7. Sharma RS, Arya AK, Rao YK. Clinico-epidemiological profile of hemophilia with special reference to development of inhibitors in Indian scenario: a cross-sectional study at tertiary care centre in north India. Int J Contemp Pediatr. 2016;3(3):922–5.
8. Hospital OS, Hospital J, Infirmary ER. Early factor VIII exposure and subsequent inhibitor development in children with severe haemophilia A. Haemophilia. 2007; 13:149–55.
9. Gouw SC, Bom JG Van Der, Berg HM Van Den, Study C. Treatment-related risk factors of inhibitor development in previously untreated patients with hemophilia A: the CANAL cohort study. Blood. 2007;109(11):4648–54.