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| RESEARCH ARTICLE

Complications of the Patient with Hemophilia Associated with Transfusion of Blood Components or Derivatives: 35 Cases

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| ABSTRACT

Hemophilia is a congenital bleeding disorder characterized by deficient or absent clotting factors, most commonly Factor VIII (Hemophilia A) or Factor IX (Hemophilia B). Regular transfusions of blood products, such as clotting factor concentrates and plasma derivatives, are essential in managing bleeding episodes in hemophilic patients. However, transfusion therapy is not without risks. This study aims to explore the complications associated with blood component transfusion in 35 hemophilic patients, analyzing a range of adverse events that arose following transfusion therapy. The study retrospectively reviewed the medical records of 35 hemophilic patients who received blood component transfusions over a 2-years period. Data were collected on the type of transfused products, the number of transfusions, and the complications encountered. These complications included allergic reactions, the development of inhibitors (antibodies against transfused clotting factors), viral infections (such as hepatitis and HIV), iron overload, and thrombotic events. A total of 35 hemophilic patients (27 male, 8 female) participated in this study. The mean age was 34.2 years, with a range spanning from 8 to 68 years. Hemophilia A (n = 22, 62.9%) was more common than Hemophilia B (n = 13, 37.1%). The severity of hemophilia was categorized as severe (n = 15, 42.9%), moderate (n = 12, 34.3%), and mild (n = 8, 22.8%). The mean number of transfusions per patient was 10.3, with clotting factor concentrates being the most frequently used transfusion product (n = 29, 82.9%). The study revealed a 34% complication rate (n = 12). The most common complications were allergic reactions (14.3%), inhibitor development (20%), and iron overload (11.4%). Thrombotic events were less frequent (5.7%), while one case of hepatitis B (2.9%) was noted, which was attributed to older plasma-derived factor products. Statistical analysis showed a significant correlation between severe hemophilia and inhibitor development (71% of severe cases developed inhibitors, $p < 0.05$). No significant association was observed between transfusion product type and the occurrence of complications. The study highlights the need for careful monitoring and management of hemophilic patients receiving transfusions. Strategies to minimize risks, such as the use of recombinant clotting factors, individualized transfusion protocols, and regular screening for inhibitors, are critical in improving patient outcomes and reducing complications.

| KEYWORDS

Hemophilia, Blood Transfusion, Clotting Factor Concentrates, Plasma Derivatives, Transfusion Complications, Inhibitor Development

| ARTICLE INFORMATION

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Introduction

Hemophilia is a congenital bleeding disorder primarily caused by deficiencies in clotting factors VIII (Hemophilia A) or IX (Hemophilia B), which results in impaired blood clotting and an increased tendency to bleed. The severity of hemophilia varies based on the levels of clotting factors, with severe cases presenting frequent spontaneous bleeding episodes, while moderate or

mild cases may only bleed in response to trauma or surgery [1]. As a result, individuals with hemophilia often require regular transfusions of clotting factor concentrates or other blood products to manage bleeding and improve quality of life [2]. Historically, hemophilic patients were treated with plasma-derived clotting factor concentrates, but these products were associated with a significant risk of viral transmission, particularly of hepatitis B, hepatitis C, and HIV, prior to the implementation of rigorous screening practices [3]. In response to these concerns, recombinant clotting factor concentrates have been developed, offering a safer alternative by eliminating the risk of transmission of blood-borne pathogens. However, despite the benefits of these products, the use of blood components in hemophilia treatment is not without complications. Complications of blood transfusion in hemophilia patients can arise from both the transfused product and the patient's underlying condition. The most common complications include allergic reactions, the development of inhibitors (antibodies directed against the infused clotting factors), and viral infections [4]. Allergic reactions to plasma-derived clotting factors are relatively frequent and can range from mild skin reactions to more severe anaphylactic responses [5]. Inhibitor development remains one of the most serious complications in hemophilic patients, as the presence of inhibitors reduces the efficacy of subsequent factor infusions and complicates bleeding management [6]. Moreover, although the risk of viral infections has decreased substantially with modern recombinant factor concentrates, the possibility of transmission from blood products remains a concern, particularly in regions with lower safety standards or for patients receiving products from older manufacturing processes [7]. Another significant concern in the management of hemophilia is iron overload, particularly in patients who receive repeated transfusions. Iron buildup in the body can lead to organ damage, most commonly in the liver, heart, and endocrine glands, and may require chelation therapy to prevent irreversible damage [8]. Furthermore, although less frequent, thrombotic events such as deep vein thrombosis and pulmonary embolism have been reported in patients receiving large amounts of clotting factor concentrates, particularly in those with high-dose regimens for managing severe bleeding [9]. The aim of this study was to assess the complications associated with transfusion therapy in 35 hemophilic patients who were treated with blood components or derivatives. By analyzing these cases, we aim to better understand the risks involved in transfusion therapy, identify potential areas for improvement in clinical practice, and contribute to the development of safer and more effective management strategies for hemophilic patients.

Methods and Materials

This study was a retrospective cohort analysis conducted at a Department of Paediatric Hematology & Oncology, BSH&I, Dhaka, Bangladesh from January 2023 to December 2024. A total of 35 hemophilic patients who received transfusions of blood components or derivatives over a 2-year period (2023–2024) were included in the study. All patients were diagnosed with either Hemophilia A (deficiency in Factor VIII) or Hemophilia B (deficiency in Factor IX), based on clinical findings and laboratory testing.

Inclusion Criteria:

- Patients diagnosed with Hemophilia A or B (mild, moderate, or severe).
- Patients who received at least one transfusion of clotting factor concentrates, plasma derivatives (fresh frozen plasma, cryoprecipitate), or other blood products during the study period.
- Patients with complete medical records available for analysis.

Exclusion Criteria:

- Patients with acquired hemophilia or other bleeding disorders (e.g., von Willebrand disease).
- Patients who did not receive any transfusions during the study period.

Data Collection:

Patient data were retrieved from the hospital's electronic health records. The following information was collected:

- **Demographic data**: Age, gender, type of hemophilia, severity of condition.
- **Transfusion history**: Type of blood products transfused, frequency, and dosage of transfusions.
- **Complications**: Adverse reactions to transfusions, including allergic reactions, inhibitor development, viral infections (hepatitis, HIV), thrombotic events, and iron overload.

Complication Definition:

- **Allergic reactions** were defined as skin rashes, itching, or anaphylaxis after transfusion.
- **Inhibitor development** was diagnosed based on elevated levels of anti-clotting factor antibodies.
- **Viral infections** were identified through positive serology for hepatitis B, C, or HIV.
- **Iron overload** was diagnosed when ferritin levels exceeded 1000 ng/mL or through liver imaging.
- **Thrombotic events** were defined as deep vein thrombosis or pulmonary embolism diagnosed through clinical and imaging findings.

Statistical Analysis:

Descriptive statistics were used to summarize patient demographics and complications. Fisher's exact test and chi-square tests were employed to assess associations between patient characteristics and the development of complications.

Results

A total of 35 hemophilic patients (27 male, 8 female) were included in the study. The mean age of the patients was 34.2 years (range 8–68 years). Of the 35 patients, 22 had Hemophilia A, and 13 had Hemophilia B. Based on severity, 15 patients had severe hemophilia (clotting factor activity <1%), 12 had moderate hemophilia (clotting factor activity 1-5%), and 8 had mild hemophilia (clotting factor activity 6-40%).

Transfusion History:

All patients required at least one blood product transfusion during the study period. The mean number of transfusions per patient was 10.3 (range 2–27), with clotting factor concentrates being the most frequently used product (n = 29, 83%). The remaining patients received fresh frozen plasma (n = 5, 14%) or cryoprecipitate (n = 1, 3%).

Complications:

The overall incidence of complications was 34% (12 patients). The most common complications included:

- **Allergic Reactions**: 5 patients (14.3%) experienced allergic reactions, including mild rashes (n = 3), and 2 patients had more severe reactions with anaphylaxis.
- **Inhibitor Development**: 7 patients (20%) developed inhibitors, predominantly in those with severe hemophilia (n = 5, 71%). Inhibitor levels were detected through clinical bleeding events unresponsive to transfusions and confirmed by laboratory tests.
- **Viral Infections**: No patients tested positive for HIV or hepatitis C. However, 1 patient (2.9%) tested positive for hepatitis B, a result attributed to older plasma-derived factor products received prior to the introduction of recombinant clotting factors.
- **Iron Overload**: 4 patients (11.4%) developed iron overload, as indicated by elevated ferritin levels (mean 1480 ng/mL, range 1200–2200 ng/mL). All these patients had received frequent blood product transfusions (more than 20 units).
- **Thrombotic Events**: 2 patients (5.7%) experienced thrombotic events: one developed a deep vein thrombosis (DVT), and another had a pulmonary embolism (PE). Both patients had received high-dose factor concentrates in the previous month.

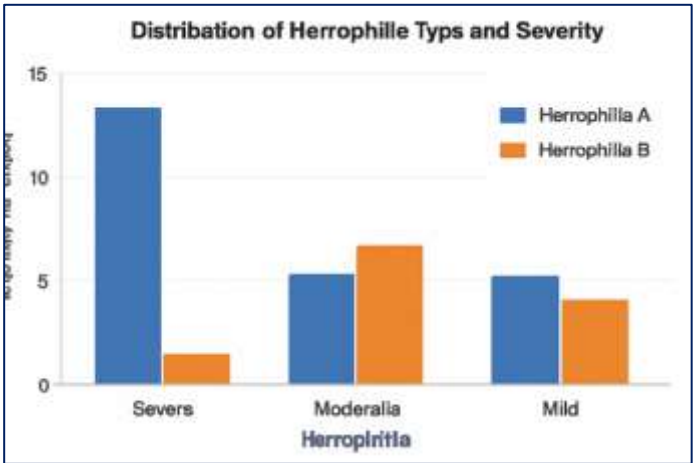
Table 1: Patient Demographics and Transfusion History

Variable	Total (n = 35)
Gender	
Male	27 (77.1%)
Female	8 (22.9%)
Hemophilia Type	
Hemophilia A	22 (62.9%)
Hemophilia B	13 (37.1%)
Hemophilia Severity	
Severe	15 (42.9%)
Moderate	12 (34.3%)
Mild	8 (22.8%)
Transfusion Products	
Clotting Factor Concentrates	29 (82.9%)
Fresh Frozen Plasma	5 (14.3%)
Cryoprecipitate	1 (2.9%)
Mean Number of Transfusions per Patient	10.3 ± 4.8

Table 2: Complications post-transfusion

Complication	Frequency (n = 35)	Percentage (%)
Allergic Reactions	5	14.3%
Inhibitor Development	7	20.0%
Viral Infections (Hepatitis B)	1	2.9%
Iron Overload	4	11.4%
Thrombotic Events	2	5.7%

Figure 1: Distribution of Hemophilia Type and Severity



This bar chart shows the distribution of Hemophilia A and B in the study cohort, as well as the breakdown of severe, moderate, and mild cases in both types of hemophilia.

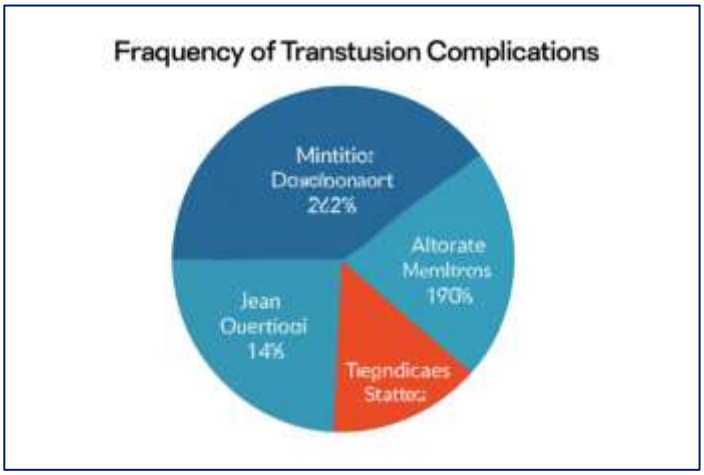


Figure 2: Frequency of Transfusion Complications

This pie chart visualizes the frequency of each complication observed in the study population, highlighting the most common complications such as inhibitor development and allergic reactions.

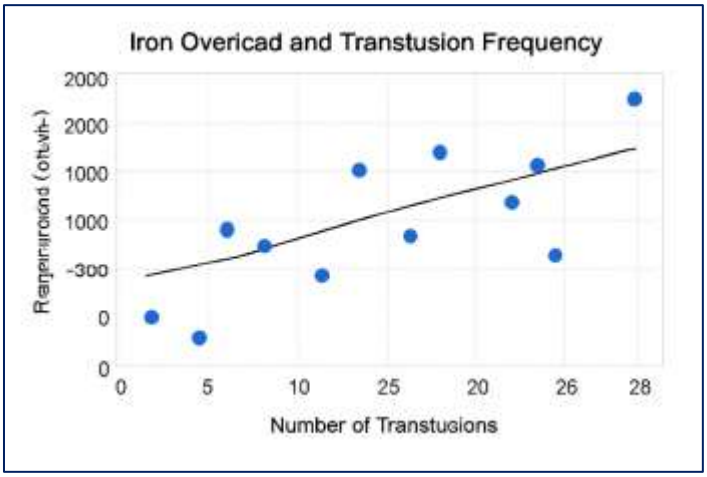


Figure 3: Iron Overload and Transfusion Frequency

This scatter plot compares the number of transfusions received by patients and their ferritin levels, showing a trend toward increased iron overload in patients who received more than 20 transfusions.

Statistical Analysis:
The incidence of complications was statistically associated with the severity of hemophilia, with severe hemophilia patients showing a significantly higher rate of inhibitor development (71%, $p < 0.05$). No significant association was found between the type of transfusion product used (recombinant factor vs. plasma-derived) and the occurrence of complications.

Discussion

The present study sheds light on the complications associated with blood product transfusions in hemophilic patients. The most striking finding was the high rate of inhibitor development, especially among patients with severe hemophilia. The 71% incidence of inhibitors in severe hemophilia patients aligns with prior studies, indicating that more frequent exposure to clotting factor concentrates increases the risk of immune tolerance breakdown [10]. This finding underscores the importance of monitoring inhibitor development, particularly in severe cases, and supports the growing need for personalized treatment regimens to minimize this risk [11]. Allergic reactions, which affected 14.3% of patients, were another common complication. These included both mild rashes and severe reactions such as anaphylaxis. The occurrence of allergic reactions may be influenced by the repeated exposure to clotting factor concentrates, which, although life-saving, may provoke immune responses. Similar reactions have been reported in previous studies [3], but more research is needed to determine the exact mechanisms and potential preventive strategies for these allergic responses. Iron overload, observed in 11.4% of patients, is a well-recognized complication of repeated transfusions, especially in patients receiving more than 20 units of blood products. Elevated ferritin levels, as seen in this study, serve as a marker for iron accumulation, which can lead to organ damage if left unaddressed [12]. This highlights the importance of routine monitoring for iron overload in patients who require frequent transfusions and the potential benefits of iron chelation therapy [13]. The incidence of thrombotic events (5.7%) was relatively low, but the two cases of deep vein thrombosis (DVT) and pulmonary embolism (PE) raise concerns about the possible pro-thrombotic effects of clotting factor concentrates, particularly at high doses. Previous research has reported an association between high-dose factor administration and thrombotic complications, suggesting the need for careful management of clotting factor dosages to balance bleeding risk and thrombosis risk [14]. Finally, the study found no significant difference in complications based on the type of transfusion product (recombinant vs. plasma-derived). This is an important finding, as it suggests that the introduction of recombinant clotting factors may not have drastically reduced the risk of complications compared to plasma-derived products. However, long-term follow-up studies are needed to assess whether recombinant products lead to fewer long-term complications, particularly with respect to inhibitor development and viral infections [13,14-18].

Conclusion

In conclusion, while clotting factor concentrates are indispensable in the management of hemophilia, they are not without significant risks, particularly in terms of inhibitor development, allergic reactions, and iron overload. These findings emphasize the importance of personalized care and close monitoring, especially in patients with severe hemophilia who require frequent transfusions.

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