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Overview of the storage duration of the packed red cell, thrombocyte concentrate, and fresh frozen plasma in transfusion reactions at Ngoerah Hospital Denpasar

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ABSTRACT

Introduction: Blood transfusion services are an integral part of healthcare efforts aimed at curing diseases and restoring health. Each blood component requires specific storage conditions and durations to maintain its efficacy. Blood components that are foreign to the recipient may trigger transfusion reactions. Data on transfusion reactions in Indonesia remains limited. However, several studies have found a significant association between the storage duration of blood products and the incidence of transfusion reactions. This study aimed to provide a comprehensive overview of the storage duration of packed red cells (PRC), thrombocyte concentrate (TC), and fresh frozen plasma (FFP) in cases of transfusion reactions.

Methods: This research is a descriptive cross-sectional study utilizing data from medical records and transfusion reaction reports at Ngoerah Hospital, Denpasar, from 2022 to 2023.

Results: Transfusion reactions occurred in 0.18% of PRC, 0.13% of TC, and 0.28% of FFP transfusions. Among transfusion reactions related to PRC, 58.9% had a storage duration of 0–7 days, with allergic reactions being the most common (54.7%), followed by febrile non-hemolytic transfusion reactions (FNHTR) at 44.2%. For TC, transfusion reactions occurred in units stored for ≤2 days (56.7%) and >2 days (43.3%), with allergic reactions accounting for 66.7% of cases. In FFP transfusions, 71.4% of reactions occurred with a storage duration of ≤30 days and all reactions were allergic in nature.

Conclusion: Transfusion reactions occur more frequently with shorter storage duration in PRC, TC, and FFP components. This may be due to the infrequent use of blood products with longer storage durations.

Keywords: Fresh frozen plasma (FFP), packed red cells (PRC), storage duration, thrombocyte concentrate (TC), transfusion reactions

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INTRODUCTION

Blood transfusion services are a form of healthcare that utilizes human blood as a basic material for humanitarian purposes and not for commercial gain. As one of the medical efforts aimed at curing diseases and restoring health, blood transfusion services require an adequate, safe, accessible, and affordable supply of blood or blood components for the community.[1] Each blood component is used for different indications; thus, separating components maximizes the utility of a single unit of whole blood.[2] Blood components that can be obtained from one unit of whole blood include red cell concentrate or packed red cell (PRC), platelet concentrate or thrombocyte concentrate (TC), fresh frozen plasma (FFP), cryoprecipitate, leukocyte-depleted red blood cell concentrate, granulocyte concentrate, single donor plasma, fibrinogen concentrate, and factor VIII concentrate.[3]

Different blood components require distinct storage conditions and temperature requirements to maintain therapeutic effectiveness. Foreign blood components may cause adverse effects in recipients, ranging from mild allergic manifestations to severe transfusion reactions. These reactions are generally triggered by plasma proteins, leukocytes, erythrocyte antigens, plasma, and other pathogens.[2]

Transfusion reactions can be categorized as acute, occurring during or shortly after transfusion, or delayed, manifesting days to weeks later. These reactions may be of immunologic or non-immunologic origin. The most frequently reported clinical manifestations include fever, chills, urticaria, and pruritus. While some of these symptoms may resolve spontaneously or with minimal intervention, the presence of respiratory distress, high-grade fever, hypotension, or hemoglobinuria may indicate a more severe transfusion reaction that requires immediate clinical attention.[4]

Data on transfusion reaction incidence in Indonesia remain limited. A study at Wahidin Sudirohusodo General Hospital Makassar recorded 93 transfusion reaction events between

January and June 2014, with 43 patients (46.2%) experiencing acute transfusion reactions.[5] Another study at Dr. Cipto Mangunkusumo Hospital Jakarta from January to December 2017 reported that transfusion reactions occurred in 288 patients (0.5%) out of 57,227 patients who received blood transfusions. In that study, the blood component most commonly associated with transfusion reactions was PRC (51.4%), followed by TC (43.4%), FFP (4.2%), and cryoprecipitate (1.0%).[6]

Biochemical, structural, and functional changes during storage can reduce oxygen delivery to tissues, while the release of extracellular vesicles and cell-free DNA may lead to a hypercoagulable state. Observational studies have shown that prolonged blood storage is oftenassociated with an increased risk of cardiovascular events.[7] A study conducted at Dr. Kariadi Hospital Semarang by Alamsyah et al. concluded that there was a significant relationship between the storage duration of PRC and the incidence of transfusion reactions ($p<0.001$), with febrile non-hemolytic transfusion reaction (FNHTR) being the most frequently reported.[8]

A study by Inaba et al. also found that critically ill trauma patients who received TC stored for 5 days experienced more complications, including a higher incidence of sepsis (16.4% developed sepsis compared to 9.2% in the group with 4-day storage and 5.5% in the group with storage duration ≤ 3 days, with a p-value of 0.033).[9]

To date, no published studies have examined the storage duration of PRC, TC, and FFP, nor their association with transfusion reactions at Ngoerah Hospital, Denpasar. Therefore, this study aimed to provide a comprehensive overview of the storage duration of PRC, TC, and FFP in relation to reported transfusion reactions at this institution.

METHODS

Study Design

This study is a descriptive cross-sectional design to provide an overview of the storage duration of PRC, TC, and FFP in reported transfusion reactions. The study was conducted using retrospective data obtained from medical records and transfusion reaction reports.

Table 1. Sample size and incidence of transfusion reactions based on blood groups

	Total	Transfusion reactions n (%)
Blood products		
PRC	51,913	95 (0.18%)
TC	23,701	30 (0.13%)
FFP	2,534	7 (0.28%)
Blood group A positive		
PRC	9,521	20 (0.21%)
TC	4,291	5 (0.12%)
FFP	509	0 (0%)
Blood group B positive		
PRC	16,242	34 (0.21%)
TC	7,335	9 (0.12%)
FFP	829	2 (0.24%)
Blood group O positive		
PRC	23,711	37 (0.16%)
TC	11,357	14 (0.12%)
FFP	1,089	3 (0.27%)
Blood group AB positive		
PRC	2,439	4 (0.16%)
TC	718	1 (0.14%)
FFP	107	2 (1.87%)

Fresh frozen plasma (FFP), packed red cells (PRC), thrombocyte concentrate (TC)

Study Setting and Period

This study was conducted at the Blood Transfusion Unit of Ngoerah Hospital, Denpasar, Indonesia. Ngoerah Hospital is a major referral center with a comprehensive transfusion service supporting various clinical departments. The study covered two years, from year 2022 to 2023.

Population and Sampling

The study sample comprised all transfusion reaction cases involving PRC, TC, and FFP blood products issued by the Blood Transfusion Unit of Ngoerah Hospital, Denpasar, between 2022 and 2023. The inclusion criteria were reported transfusion reaction cases, while the exclusion criteria were incomplete transfusion reaction data. Data collection was performed using a total sample of transfusion reaction cases that occurred during 2022–2023.

Data Analysis

Descriptive statistical methods were used to summarize the characteristics of transfusion reactions by blood component type and storage duration. Data were presented in the form of tables showing absolute numbers and percentages.

RESULTS

The data showed that transfusion reactions occurred in 95 (0.18%) out of 51,913 PRC blood products, 30 (0.13%) out of 23,701 TC blood products, and 7 (0.28%) out of 2,534 FFP blood products. The highest incidence of transfusion reactions was observed in AB-positive Rh blood group FFP products at 1.87%. In contrast, no transfusion reactions were observed in FFP products from individuals with the positive Rh blood group. The sample size and incidence of transfusion reactions, categorized by blood group, are presented in **Table 1**.

The characteristics of transfusion reaction incidents in the PRC, TC, and FFP, based on age, gender, source of blood products (Palang Merah Indonesia, PMI; and the blood transfusion unit of Ngoerah Hospital), as well as compatibility test results, are presented in **Table 2**.

Based on the storage duration of PRC and the occurrence and types of transfusion reactions, the data are presented in **Table 3**. The majority of PRC blood products associated with transfusion reactions had a storage duration of 0–7 days (58.9%). The most common type of transfusion reaction in PRC products was allergic reactions (54.7%), with FNHTR at 44.2%.

Based on the storage duration of TC and the occurrence and types of transfusion reactions, the data are presented in **Table 4**. Transfusion reactions in TC blood products occurred in units stored for ≤ 2 days at a rate of 56.7% and in units stored for> 2 days at a rate of 43.3%. The most common type of transfusion reaction in TC products was allergic reaction (73.3%).

Based on the storage duration of FFP and the occurrence and types of transfusion reactions, the data are presented in **Table 5**. The majority of transfusion reactions associated with FFP blood products occurred within a storage duration of ≤ 30 days (71.4%). Allergic reactions were the type of transfusion reaction observed in all FFP blood products that caused transfusion reactions in patients.

Table 2. Characteristics of transfusion reaction incidents in PRC, TC, and FFP

Characteristics	PRC (n=95)	TC (n=30)	FFP (n=7)
Age (years), mean ± SD	39.89 ± 24.57	30.40 ± 23.72	43.19 ± 25.06
Gender, n (%)			
Male	47 (49.5%)	14 (46.7%)	5 (71.4%)
Female	48 (50.5%)	16 (53.3%)	2 (28.6%)
Source of blood products, n (%)			
PMI	55 (57.9%)	16 (53.3%)	1 (14.3%)
Blood transfusion unit	40 (42.1%)	14 (46.7%)	6 (85.7%)
Crossmatch results, n (%)			
Compatible	77 (81.1%)	25 (83.3%)	7 (100%)
Incompatible	18 (18.9%)	5 (16.7%)	0 (0%)

Fresh frozen plasma (FFP), packed red cells (PRC), thrombocyte concentrate (TC), Palang Merah Indonesia (PMI), standard deviation (SD)

Table 3. Storage duration and types of transfusion reactions in PRC

Storage duration and types of transfusion reactions	(n=95)
Storage duration, n (%)	
0 – 7 days	56 (58.9%)
8 – 14 days	34 (35.8%)
> 14 days	5 (5.3%)
Types of transfusion reactions, n (%)	
FNHTR	42 (44.2%)
Allergic reaction	52 (54.7%)
Other reactions	1 (1.1%)

Febrile non-hemolytic transfusion reactions (FNHTR)

Table 4. Storage duration and types of transfusion reactions in TC

Storage duration and types of transfusion reactions	(n=30)
Storage duration, n (%)	
≤ 2 days	17 (56.7%)
> 2 days	13 (43.3%)
Types of transfusion reactions, n (%)	
FNHTR	6 (20.0%)
Allergic reaction	22 (73.3%)
TRALI	2 (6.7%)

Febrile non-hemolytic transfusion reactions (FNHTR), Transfusion-Related Acute Lung Injury (TRALI)

Table 5. Storage duration and types of transfusion reactions in FFP

Storage duration and types of transfusion reactions	(n=7)
Storage duration, n (%)	
≤ 30 hari	5 (71.4%)
> 30 hari	2 (28.6%)
Types of transfusion reactions, n (%)	
Allergic reaction	7 (100%)

DISCUSSION

This study found that PRC blood products were the most common cause of transfusion reactions, followed by TC and FFP. Similar results were reported in a study at Dr. Cipto Mangunkusumo Hospital, Jakarta, which showed that the blood product most frequently causing transfusion reactions was PRC (51.4%), followed by TC (43.4%), FFP (4.2%), and cryoprecipitate (1.0%).[6] This is likely because PRC is the most commonly transfused blood product.

However, based on the incidence of transfusion reactions per blood product, this study showed a higher rate of transfusion reactions in FFP (0.28%) compared to PRC (0.18%) and TC (0.13%). In contrast, a study in Japan found a higher incidence of TC (3.8%) compared to FFP (1.3%) and PRC (0.6%).[10] Meanwhile, another study in India revealed the highest incidence of transfusion reactions in patients receiving PRC (1.4%) and FFP (0.6%), with no transfusion reactions occurring in patients receiving TC.[11] These differences suggest that various factors, including patient ethnicity and clinical diagnosis, may influence transfusion reactions.

Overall, this study found that allergic reactions were the most common manifestation of acute transfusion reactions. These were followed by FNHTR, with a small proportion resulting in TRALI, which was observed in TC blood products. This finding aligns with the study by Payandeh et al. in 2013, which reported that the most common acute transfusion reactions were allergic reactions with various manifestations such as urticaria, rash, and itching (49.2%), followed by FNHTR (37.2%), while other reactions included pain at the transfusion site (6.8%) and hypotension (6.8%).[12] In contrast, a study by Bassi et al. in India in 2017 found FNHTR to be the most common type of transfusion reaction, surpassing allergic reactions.[13]

At the Ngoerah Hospital, PRC blood products use CPDA-1 anticoagulant, allowing a storage period of 35 days. Storage of PRC blood products at a standard temperature of 2°C to 6°C aims to enhance the stability of PRC. After 14 days of storage, byproducts from glycolytic metabolism, such as lactic acid and protein, accumulate, leading to structural and functional changes in the cells over time.[8] Based on the results, most transfusion reactions occurred in PRC blood products stored for 0–7 days (58.9%), followed by 8–14 days (35.8%) and >14 days (5.3%). This is because the majority of transfused PRC products did not exceed the 7-day storage period.

Several previous studies have shown that cytokines with immunoinflammatory effects are considered mediators of FNHTR. The cytokines involved include TNF-α, IL-1, IL-6, and IL-8, which originate from stored blood products. The longer the storage duration, the higher the levels of cytokines.[14] In this study, the incidence of transfusion reactions in PRC products stored for more than 14 days was only 5.3%. This may be due to the high demand for PRC blood products at Ngoerah Hospital, making the use of PRC products with longer storage durations very rare.

TC blood products at the Ngoerah Hospital are stored in an agitator at temperatures between 20°C and 24°C, with a storage period of 5 days. According to the study results, transfusion reactions in TC blood products stored for ≤ 2 days accounted for 56.7%, while those stored for > 2 days accounted for 43.3%.

The most frequent transfusion reaction found in TC blood products in this study was allergic reactions. Several studies have found that allergic reactions can occur without allergen involvement, especially in TC. Stored TC blood products contain accumulated inflammatory cytokines and chemokines, which directly bind to receptors on mast cells and basophils, known as biological response modifiers (BRMs), including vascular endothelial growth factor, sCD40 ligand, and transforming growth factor-β1. The accumulation of bioactive and proinflammatory products during the collection, production and storage of TC blood products can induce immune responses and transfusion reactions in patients.[6,14] Febrile non-hemolytic transfusion reactions occurring in TC blood products may also be related to storage, involving the production and release of biologically active cytokines by leukocytes present in the TC component.[4]

In this study, transfusion reactions were more frequently observed with TC blood products stored for ≤ 2 days, although the difference in incidence compared to products stored for > 2 days was small. This may also be due to the high demand for TC blood products at Ngoerah Hospital and the short storage duration of TC products.

FFP products at the Ngoerah Hospital are stored at temperatures between -30°C and -39°C, with a maximum storage duration of 12 months. Based on the study results, transfusion reactions occurred in 71.4% of FFP products stored for ≤ 30 days and 28.6% in those stored for > 30 days.

The transfusion reactions observed in FFP products in this study were allergic reactions. Allergic reactions occur when recipient IgE antibodies bind to donor allergens, triggering the release of mediators from mast cells. Known allergens include donor plasma proteins, chemical allergens (such as methylene blue in FFP preparations), and food allergens. Allergic reactions can also result from passive antibody transfer and sensitization, occurring when blood products containing specific IgA and IgE antibodies are transfused to the patient.6 Methylene blue is a reagent used for viral inactivation in FFP but has been reported to cause anaphylactic shock after transfusion.[15] In this study, the FFP preparations did not use methylene blue.

Another transfusion reaction associated with FFP products and storage duration is FNHTR, which is suspected to be caused by an immune response to leukocytes in the blood. This transfusion reaction is linked to leukocytes contaminating the plasma that survives the freeze-thaw process.[4] However, FNHTR was not observed in this study.

Transfusion reactions based on compatibility testing in this study mostly showed compatible results. Compatibility testing is performed to detect antibodies in the patient's plasma that can destroy transfused erythrocytes, as well as antibodies in donor plasma that may enter the patient's body.[16] The purpose of compatibility testing is to detect ABO incompatibility, which is the most common cause of acute hemolytic transfusion reaction (AHTR).[17] According to this study, AHTR did not occur. Compatibility testing is also conducted to detect alloantibodies and autoantibodies.

This study presented several limitations. The data derived from a single tertiary care center over two years may limit the generalizability of the findings to other settings with different transfusion practices and patient populations. Thus, mild or subclinical reactions may have been underreported, potentially resulting in an underestimation of the true incidence.

CONCLUSION

Transfusion reactions occur more frequently with shorter storage durations in PRC, TC, and FFP components. This is likely due to the very rare use of blood products with longer storage durations. Further multicenter, prospective studies, and randomized trials comparing different storage durations are needed to confirm and clarify these findings. Additionally, investigating patients' specific risk factors will support the development of personalized transfusion protocols aimed at reducing adverse events.

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None.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest related to this study.

AUTHOR CONTRIBUTION

All authors contributed equally to this work.

ETHICS CONSIDERATION

Ethical clearance for this study was obtained from the Research Ethics Committee, Faculty of Medicine, Universitas Udayana (Approval No. 1310/UN14.2.2.VII.14/LT/2024).

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