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EFFECT OF DONOR COMPONENT AND RECIPIENT CHARACTERISTICS ON HAEMOGLOBIN INCREMENT FOLLOWING RCC TRANSFUSION IN ICU PATIENTS

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Abstract

Background:

Anemia is highly prevalent among critically ill patients, and red cell concentrate (RCC) transfusion is frequently used in the intensive care unit, although the hemoglobin response remains variable. This study aimed to evaluate the influence of donor component characteristics and recipient clinical factors on hemoglobin increment following RCC transfusion in ICU patients at a resource-limited tertiary care hospital in Pakistan. This will provide context-specific evidence to optimize transfusion practices and improve patient blood management in critically ill populations.

Materials and Methods:

This prospective observational cohort study was conducted in an adult intensive care unit at Federal Government Polyclinic Hospital, Islamabad, from September 2024 to February 2025, enrolling 150 patients who received red cell concentrate (RCC) transfusion and had standardized pre- and post-transfusion hemoglobin measurements. Recipient clinical variables and donor/component characteristics were collected prospectively, and hemoglobin increment at 24 hours was analyzed using univariable and multivariable regression models. All data was entered and calculated using SPSS version 23.0. The statistical significance set at $p \leq 0.05$.

Results:

Among 150 ICU patients receiving a single unit of red cell concentrate, the mean hemoglobin increment at 24 hours was 0.96 ± 0.42 g/dL, with substantial interpatient variability. Fresher blood (≤14 days), Rh-positive units, younger donor age, and absence of active bleeding were associated with significantly greater hemoglobin increments, while donor sex, sepsis, and vasopressor use were not. On multivariable analysis, active bleeding, higher pre-transfusion hemoglobin, increasing storage duration, donor age, and Rh status independently predicted hemoglobin response.

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Conclusion:

Hemoglobin response to red cell concentrate transfusion in ICU patients is influenced by recipient and donor factors, including active bleeding, baseline hemoglobin, storage duration, donor age, and Rh status. Recognizing these determinants can optimize transfusion decisions and blood utilization, especially in resource-limited settings.

INTRODUCTION

Anemia is a common finding among critically ill patients and is frequently encountered during intensive care unit (ICU) admission.[1] It results from a combination of factors, including acute blood loss, hemodilution, inflammation-mediated suppression of erythropoiesis, nutritional deficiencies, and frequent phlebotomy.[2] As anemia has been associated with impaired oxygen delivery and adverse clinical outcomes, red cell concentrate (RCC) transfusion remains one of the most commonly performed therapeutic interventions in the ICU setting.[3]

Despite its widespread use, the clinical response to RCC transfusion, particularly the expected rise in hemoglobin concentration, varies considerably among critically ill patients.[4] Conventionally, transfusion of one unit of RCC is expected to increase hemoglobin by approximately 1 g/dL in stable adults; however, this assumption is often unreliable in ICU populations.[5] Multiple physiological and pathological factors unique to critical illness, such as ongoing blood loss, fluid shifts, capillary leak, inflammation, and altered red cell survival, may attenuate the hemoglobin increment following transfusion.[6] Consequently, understanding the determinants of transfusion efficacy has become an area of growing clinical interest.

Both recipient-related factors and donor or blood component characteristics have been proposed to influence post-transfusion hemoglobin response.[7] Recipient factors such as baseline hemoglobin concentration, active bleeding, sepsis, vasopressor use, and severity of illness may affect red cell distribution and survival. In parallel, donor-related variables including donor age, sex, blood group, and storage duration of RCC units have been increasingly studied for their potential impact on transfusion outcomes.[4,7] Prolonged storage of red blood cells has been associated with biochemical and structural changes, collectively termed "storage lesions," which may impair red cell deformability, reduce post-transfusion survival, and limit effective hemoglobin increment.[8]

Several studies from high-income countries have examined the relationship between storage duration and clinical outcomes, including hemoglobin increment, transfusion requirements, and mortality, with mixed results.[9] While some investigations have demonstrated reduced hemoglobin response with older stored blood, others have failed to show clinically meaningful differences.[10] Similarly, emerging evidence suggests that donor characteristics such as age and sex may influence red cell quality and post-transfusion performance, although data remain limited and inconsistent.[7,11] Importantly, most of the available literature originates from well-resourced healthcare systems with standardized transfusion practices, leukoreduced blood products, and strict inventory management, limiting the generalizability of these findings to low- and middle-income countries.[8,12]

In resource-limited settings such as Pakistan, transfusion practices differ substantially due to constraints in blood supply, storage infrastructure, and routine component modification.[13] Blood products are often transfused based on availability rather than optimal donor or storage characteristics, and routine leukoreduction is not universally practiced.[14] Furthermore, critically ill patients in such settings frequently present with advanced disease, delayed access to care, and higher prevalence of active bleeding and sepsis all of which may further influence transfusion efficacy.[15,16] Despite the high burden of critical illness and frequent use of blood transfusion in ICUs across Pakistan, local data evaluating the

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determinants of hemoglobin increment following RCC transfusion are scarce.

Understanding how donor component variables and recipient clinical characteristics affect hemoglobin response in critically ill patients is essential for optimizing transfusion practices, minimizing unnecessary transfusions, and improving patient outcomes particularly in environments where blood is a limited and costly resource.[4] Quantifying the expected hemoglobin increment under real-world ICU conditions can assist clinicians in making evidence-based transfusion decisions and may contribute to more rational utilization of blood products.

The present study was therefore designed to evaluate the effect of donor component characteristics and recipient clinical factors on hemoglobin increment following RCC transfusion in ICU patients. By systematically analyzing both donor- and recipient-related variables in a resource-limited tertiary care hospital in Pakistan, this study aims to provide context-specific evidence that may inform transfusion strategies and contribute to improved patient blood management in critically ill populations.

MATERIALS AND METHODS:

This prospective observational cohort study was conducted in the adult intensive care unit (ICU) at the Department of Medicine, at Federal Government Polyclinic Hospital, (FGPC) Islamabad after approval by the Institutional Ethics Committee. All data were anonymized to maintain participant confidentiality. The study was carried out over a period of 6 months from September 2024 to February 2025. Adult patients aged 18 years or older who received at least one unit of red cell concentrate (RCC) during their ICU stay were screened for eligibility.

Patients were included if a pre-transfusion hemoglobin measurement was available within 6 hours prior to transfusion and a post-transfusion hemoglobin measurement was obtained at 24 ± 6 hours following completion of transfusion. Patients receiving massive transfusion (defined as ≥4 units of RCC within 6 hours), exchange transfusions, intraoperative transfusions, or extracorporeal support, as well as those with documented hemolytic transfusion reactions or incomplete donor or laboratory data, were excluded. In patients who received multiple transfusions during a single ICU admission, only the first transfusion event was included in the primary analysis.

All RCC units were issued by the institutional blood bank in accordance with standard transfusion protocols and were ABO and Rh compatible. Units were stored at 2–6°C and transfused within the licensed storage period. Each unit was transfused over 2–4 hours under standard monitoring procedures.

Recipient demographic and clinical data were collected prospectively at the time of transfusion and included age, sex, ICU diagnosis, pre-transfusion hemoglobin concentration, presence of active bleeding, vasopressor support, sepsis, and renal failure. Active bleeding was defined as clinically documented ongoing blood loss or the requirement for hemostatic intervention at the time of transfusion. Sepsis was defined according to Sepsis-3 criteria. Donor and component characteristics were obtained from blood bank records and included donor age, donor sex, Rh status, storage duration of the RCC unit (days from donation to transfusion), and unit volume. All donor identifiers were anonymized prior to data analysis.

Hemoglobin concentration was measured in the hospital laboratory, with routine quality control procedures performed daily. The primary outcome was the absolute hemoglobin increment, calculated as the difference between post-transfusion and pre-transfusion hemoglobin concentrations, measured at 24 hours following RCC transfusion.

Data were entered and analyzed using IBM SPSS Statistics version 23. Continuous variables were assessed for normality and expressed as mean ± standard deviation or median with interquartile range as appropriate, while categorical variables were expressed as frequencies and percentages. Comparisons of hemoglobin increment between groups were conducted using the independent samples t-test or Mann–Whitney U test, as appropriate. Multivariable linear regression

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analysis was performed to identify independent predictors of hemoglobin increment, with inclusion of clinically relevant recipient, donor, and component variables, including pre-transfusion hemoglobin, active bleeding, storage duration, donor age, donor Rh status, unit volume, vasopressor use, and sepsis. Regression coefficients (β), 95% confidence intervals, and p-values were reported, and model performance was assessed using the coefficient of determination (R^2). A p-value of less than 0.05 was considered statistically significant.

RESULTS:

A total of 150 ICU patients receiving a single unit of red cell concentrate (RCC) were included in the analysis. Baseline recipient and donor characteristics are summarized in Table 1. The mean age of recipients was 55 ± 18 years, and 60.0% were male. The mean pre-transfusion hemoglobin concentration was 8.0 ± 1.5 g/dL. Active bleeding at the time of transfusion was documented in 25.3% of transfusion events, while 40.0% of patients had sepsis and 30.0% required vasopressor support.

Donor characteristics demonstrated a predominance of male donors (80.0%), with a mean donor age of 32 ± 10 years. The majority of transfused units were Rh-positive (80.0%), and the median storage duration was 14 days (IQR 8–22).

Table 1. Baseline recipient and donor characteristics of the study population (n = 150)

CHARACTERISTIC	VALUE
Recipient characteristics	
Age, years (mean ± SD)	55 ± 18
Male sex, n (%)	90 (60.0)
Pre-transfusion hemoglobin, g/dL (mean ± SD)	8.0 ± 1.5
Active bleeding at transfusion, n (%)	38 (25.3)
Vasopressor support, n (%)	45 (30.0)
Sepsis at time of transfusion, n (%)	60 (40.0)
Renal failure, n (%)	30 (20.0)
Donor and component characteristics	
Donor age, years (mean ± SD)	32 ± 10
Male donor, n (%)	120 (80.0)
Rh-positive units, n (%)	120 (80.0)
Storage duration, days (median [IQR])	14 [8–22]
Unit volume, mL (mean ± SD)	320 ± 25

Overall, the mean hemoglobin increment at 24 hours following transfusion was 0.96 ± 0.42 g/dL. Variability in hemoglobin response was observed across both donor and recipient characteristics (Table 2).

Transfusion of RCC units stored for ≤14 days resulted in a significantly higher hemoglobin increment compared with units stored for >14 days (1.07 ± 0.39 g/dL vs 0.84 ± 0.41 g/dL; p = 0.002). Similarly, units from donors aged ≤30 years were associated with a greater hemoglobin increment than those from donors aged >30 years (1.04 ± 0.40 g/dL vs 0.90 ± 0.43 g/dL; p = 0.031).

Recipients transfused with Rh-positive units demonstrated a modest but statistically significant increase in hemoglobin increment compared with Rh-negative units (1.00 ± 0.41 g/dL vs 0.83 ± 0.44 g/dL; p = 0.041).

Active bleeding at the time of transfusion had the most pronounced effect on hemoglobin response. Patients with active bleeding experienced a significantly lower hemoglobin increment compared with non-bleeding patients (0.62 ±

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0.36 g/dL vs 1.07 ± 0.38 g/dL; $p < 0.001$) as shown in figure 1.

No statistically significant differences in hemoglobin increment were observed with respect to donor sex, vasopressor support, or presence of sepsis at the time of transfusion.

Table 2: Hemoglobin increment at 24 hours according to donor and recipient characteristics

VARIABLE	CATEGORY	HEMOGLOBIN INCREMENT (g/dL), Mean ± SD	p-VALUE*
Storage duration	≤14 days (n = 82)	1.07 ± 0.39	0.002
	>14 days (n = 68)	0.84 ± 0.41	
Donor age	≤30 years (n = 65)	1.04 ± 0.40	0.031
	>30 years (n = 85)	0.90 ± 0.43	
Donor Rh status	Rh-positive (n = 120)	1.00 ± 0.41	0.041
	Rh-negative (n = 30)	0.83 ± 0.44	
Active bleeding	Yes (n = 38)	0.62 ± 0.36	<0.001
	No (n = 112)	1.07 ± 0.38	
Donor sex	Male vs Female	0.99 ± 0.42 vs 0.88 ± 0.40	0.090
Vasopressor support	Yes vs No	0.90 ± 0.44 vs 0.99 ± 0.40	0.210
Sepsis	Yes vs No	0.93 ± 0.43 vs 0.98 ± 0.41	0.370

* $p \leq 0.05$ was considered statistically significant.

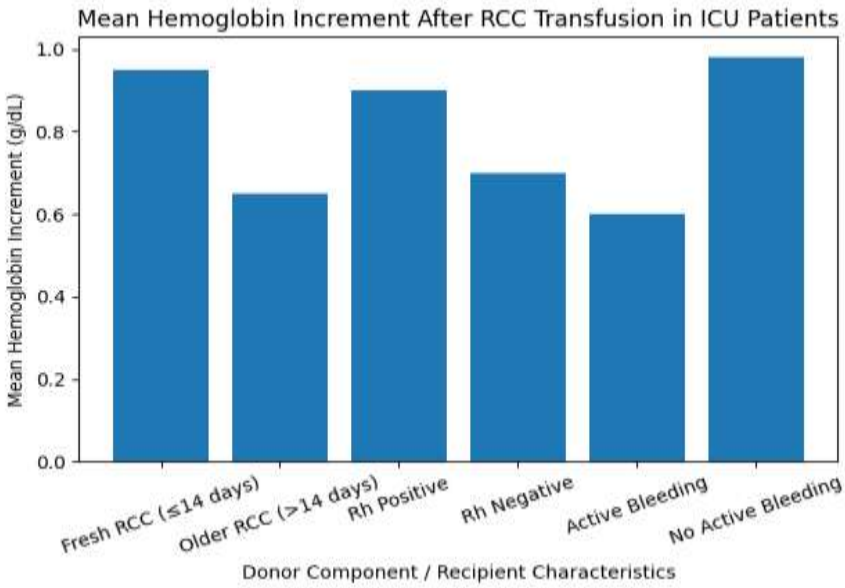


Figure 1: Mean hemoglobin increment following red cell concentrate transfusion according to donor component and recipient characteristics

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Results of the multivariable linear regression analysis are presented in Table 3. After adjustment for recipient and donor factors, several variables remained independently associated with hemoglobin increment.

Higher pre-transfusion hemoglobin concentration was inversely associated with post-transfusion hemoglobin increment (β = −0.08 g/dL per 1 g/dL increase; 95% CI −0.13 to −0.03; p = 0.002). Active bleeding was independently associated with a substantial reduction in hemoglobin increment (β = −0.39 g/dL; 95% CI −0.52 to −0.25; p < 0.001).

Increasing storage duration of RCC units was associated with a progressive decrease in hemoglobin increment (β = −0.002 g/dL per day; 95% CI −0.004 to −0.001; p = 0.004). Donor age also demonstrated a small but statistically significant inverse association with hemoglobin response (β = −0.003 g/dL per year; 95% CI −0.006 to −0.001; p = 0.028).

Transfusion of Rh-positive units was independently associated with a higher hemoglobin increment compared with Rh-negative units (β = +0.12 g/dL; 95% CI 0.01 to 0.23; p = 0.036). Unit volume, vasopressor use, and sepsis were not independently associated with hemoglobin increment after adjustment.

The final multivariable model explained 42% of the variance in hemoglobin increment (R^2 = 0.42).

Table 3. Multivariable linear regression analysis of factors associated with hemoglobin increment

VARIABLE	β COEFFICIENT (g/dL)	95% CONFIDENCE INTERVAL	p-VALUE*
Pre-transfusion hemoglobin (per 1 g/dL increase)	−0.08	−0.13 to −0.03	0.002
Active bleeding (yes vs no)	−0.39	−0.52 to −0.25	<0.001
Storage duration (per day increase)	−0.002	−0.004 to −0.001	0.004
Donor age (per year increase)	−0.003	−0.006 to −0.001	0.028
Rh-positive unit (vs Rh-negative)	+0.12	+0.01 to +0.23	0.036
Unit volume (per 10 mL increase)	+0.01	−0.01 to +0.03	0.270
Vasopressor support	−0.05	−0.17 to +0.07	0.410
Sepsis	−0.04	−0.15 to +0.07	0.480

* p ≤ 0.05 was considered statistically significant.

DISCUSSION:

In this prospective observational study of critically ill patients, we demonstrate that the hemoglobin increment following red cell concentrate (RCC) transfusion is highly variable and is independently influenced by both recipient-related and donor component characteristics. Although the mean hemoglobin increment in our cohort approximated the conventionally expected 1 g/dL, substantial heterogeneity was observed across clinical subgroups. These findings support previous observations that the traditional assumption of a predictable hemoglobin rise following transfusion is frequently unreliable in ICU populations,

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particularly in the presence of ongoing physiological derangements and blood component variability.[17,18]

Active bleeding showed the strongest independent association with reduced hemoglobin increment in our cohort, with bleeding patients experiencing a markedly attenuated post-transfusion hemoglobin rise compared with non-bleeding patients. This finding is consistent with the work of Yadav et al., who reported that ongoing blood loss and hemodilution substantially diminish transfusion efficacy in critically ill patients.[19] Similarly, Hébert et al. demonstrated that patients transfused during active hemorrhage often fail to achieve the expected hemoglobin increment due to continued losses and redistribution effects.[3] In resource-limited settings, where delayed hemostatic interventions and higher transfusion thresholds may be common, this phenomenon may be further magnified, emphasizing the importance of addressing bleeding sources prior to transfusion.

Baseline hemoglobin concentration was inversely associated with post-transfusion hemoglobin increment in our multivariable analysis, indicating that patients transfused at higher hemoglobin levels derive a smaller measurable benefit from RCC transfusion. This observation aligns with findings by Roubinian et al., who reported that transfusions administered at lower baseline hemoglobin concentrations resulted in significantly greater hemoglobin rises, likely reflecting dilutional and physiological ceiling effects at higher hemoglobin levels.[18] These data lend further support to restrictive transfusion strategies recommended by contemporary guidelines and reinforce the limited utility of transfusion at near-normal hemoglobin concentrations in critically ill patients.

Storage duration of RCC units emerged as an independent determinant of hemoglobin response in our study, with longer-stored blood associated with a significantly reduced hemoglobin increment. This finding is biologically plausible and consistent with the well-described red blood cell "storage lesion," which encompasses progressive biochemical and structural changes during storage, including membrane loss, reduced deformability, oxidative damage, and impaired microvascular flow.[8] Clinical evidence regarding the impact of storage duration on outcomes has been mixed. Systematic review summarized by Shah et al. failed to demonstrate consistent differences in major clinical outcomes.[20] Our findings suggest that while storage duration may not uniformly affect mortality, it may meaningfully influence transfusion efficiency as reflected by hemoglobin increment, an outcome of particular relevance in blood-limited settings.

Donor age was also independently associated with hemoglobin increment in our cohort, with increasing donor age correlating with a modest reduction in transfusion response. Mykhailova et al. demonstrated that donor age significantly influences the rheological properties of stored red blood cells, with units from younger donors exhibiting superior deformability and storage resilience.[21] Roubinian et al. showed no significant differences in hemoglobin increments related to donor age.[18] These biological differences may plausibly translate into improved post-transfusion survival and hemoglobin increment, as observed in our cohort.

Transfusion of Rh-positive units was associated with a higher hemoglobin increment compared with Rh-negative units. While Rh status itself has not been consistently identified as a determinant of transfusion efficacy, this association may reflect indirect factors such as donor pool composition, unit availability, or differences in storage duration rather than a direct immunohematological effect. Roubinian et al. showed positive donor or recipient Rh-D status was associated with larger hemoglobin increments compared with negative Rh-D status ($P < .001$).[18]

Markers of critical illness severity, including sepsis and vasopressor use, were not independently associated with hemoglobin increment after adjustment for confounding variables. Although sepsis has been linked to altered red cell survival and microcirculatory dysfunction, prior studies, failed to demonstrate a consistent independent effect of sepsis on

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immediate post-transfusion hemoglobin response.[18]

The implications of these findings are particularly relevant in resource-limited settings such as Pakistan, where transfusion practices are constrained by blood availability, limited inventory control, and lack of routine leukoreduction. Studies by Waheed U and Mahmood et al. have highlighted systemic challenges in transfusion services across Pakistan, including reliance on available rather than optimal blood components and variability in storage practices.[13,22] In such environments, identifying factors that most strongly influence transfusion efficacy is essential to optimize blood utilization, minimize unnecessary transfusions, and reduce exposure to potential transfusion-related complications.

Several limitations merit consideration. The single-center design may limit generalizability, and residual confounding cannot be excluded. Only ICU patients were included and hemoglobin increment in ward settings was not evaluated. Additionally, post-transfusion hemoglobin was measured at a single time point, and longer-term red cell survival was not assessed.

CONCLUSION:

Hemoglobin increment following RCC transfusion in ICU patients is determined by a complex interplay of recipient, donor, and component factors. Active bleeding, baseline hemoglobin concentration, storage duration, donor age, and Rh status independently influence post-transfusion hemoglobin response. Recognition of these factors may improve transfusion decision-making and resource utilization, particularly in settings with limited blood supply.

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