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"Observational Study of increase in Haemoglobin following packed red cell transfusion pre-operatively in Infants and Children"

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Abstract

Background: *Anemia in infants and young children is characterized by reduced hemoglobin or red blood cell mass leading to impaired oxygen delivery; it is highly prevalent worldwide, especially in low-resource settings. Clinically, affected children may show pallor, poor feeding, lethargy, delayed growth and neurocognitive development, and in severe cases tachycardia or heart failure.*

When anemia is severe or when a child requires anesthesia and surgery, optimization of oxygen-carrying capacity is critical, and packed red blood cell (PRBC) transfusion may be necessary preoperatively to raise hemoglobin to a safe level for the perioperative period.

This study aims to observe the rise in hemoglobin following preoperative packed red blood cell transfusion in infants and young children. Specifically, it will evaluate the hemoglobin response to a standard transfusion volume of 20 mL/kg, assess the influence of donor blood hematocrit on the magnitude of hemoglobin increase, and compare the measured post-transfusion hemoglobin change with the estimated increase calculated from standard formulas. It will also compare the results with previously related studies.

Methods: *Study Design: Prospective observational study. Duration: August 2022 – June 2024. Participants: 322 infants and children (1–60 months) receiving preoperative PRBC transfusions of which 199 were male and 123 were females.*

Key Variables: - Pre-transfusion Hb (mean: 7.35 g/dL), hematocrit (mean: 22%). - Donor PRBC hematocrit (mean: 59.5%). - Transfusion duration: 4 hours (210 cases), 5 hours (58 cases), 6 hours (54 cases). - Post-transfusion Hb sampling: ~6 hours (60%), ~10 hours (10%). - Transfusion reactions: 8 cases (2.48%).

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Results:

Hb Increase:
-Actual change: Mean = 3.97 g/dL, Median = 4 g/dL.
-Change as per Formula: Mean = 3.98 g/dL, Median = 3.91 g/dL.

HCT Increase:
-Actual change: Mean = 11.9 g/dL, Median = 12 g/dL.
-Change as per Formula: Mean = 11.9 g/dL, Median = 11.74 g/dL.
-Transfusion Reactions: 2.48% incidence, with no severe adverse events reported.

Conclusions:

1. *Transfusions with higher Donor Hematocrit raised more Hb with the same volume dosage.*
2. *Increase in Hb predicted through formula was closer to the actual value.*
3. *Time of Post Transfusion Sampling did not affect the change in Hb significantly.*
4. *Duration of Transfusion (4-6 hrs) did not have any serious adverse event.*

Keywords: Anemia, PRBC Transfusion, Haemoglobin, Donor Hematocirt, Infants and Children

INTRODUCTION

Children have higher metabolic rate, higher oxygen consumption and greater rates of cardiac output to circulating blood volume. [1,2]. Foetal haemoglobin (Hb F) makes up for up to 70% of total Hb in term infants as compared to 97% for pre-term neonates at birth.[3] Hb F has a higher affinity for oxygen with a consequent shift of oxygen Hb dissociation curve to the left implying decreased oxygen delivery to the tissues.

A. Hematocrit values are obtained through laboratory testing and provide valuable insights into a patient's blood composition. By measuring the percentage of RBCs in the total blood volume, hematocrit indirectly reflects Haemoglobin concentration.

PACKED RED CELLS:

A. Packed red cells, also known as packed red blood cells or packed RBCs, are blood components that consist predominantly of RBCs. PRBC transfusion is a common medical intervention employed pre-operatively in infants and children with low Haemoglobin levels to increase their oxygen-carrying capacity.

B. It involves the administration of concentrated RBCs to enhance oxygen delivery during surgery and improve post-operative outcomes. The decision to transfuse packed red cells is based on careful evaluation of the patient's clinical condition, Haemoglobin and haematocrit levels, anticipated blood loss during surgery, and the overall risk-benefit ratio.

Why Haemoglobin is preferred over Hematocrit for assessment of Transfusion?

Reasons for Preferring Hemoglobin

1. **Direct Oxygen-Carrying Assessment**: Hb directly measures oxygen transport capacity—the primary goal of transfusion. Hct indirectly reflects RBC mass and is skewed by plasma volume changes (e.g., dehydration, overhydration).

2. **Standardized Measurement**: Hb assays are highly consistent across labs. Hct values vary with techniques (centrifugation vs. automated counters) and are influenced by RBC size/shape abnormalities.

3. **Evidence-Based Thresholds**: Clinical guidelines (e.g., AABB, BCSH) define transfusion triggers using Hb (e.g., Hb <7 g/dL in stable critically ill children). Hct lacks specific transfusion thresholds.

4. **Accurate Anemia Severity**: Hb correlates linearly with oxygen delivery. Hct overestimates anemia in hypovolemia (e.g., hemorrhage) and underestimates it in hypervolemia (e.g., fluid overload).

MATERIAL AND METHODS

a. **Study Setting:** IPD at Pragna Children's Hospital.
b. **Study Design:** Observational Study, increase in hemoglobin post transfusion with fixed dosing of PRBC used for all transfusions.[20]
c. **Study Sample**: Infants and children requiring packed cell transfusion pre-operatively.
d. **Sample size:** All Infants and children who gets admitted to Pragna Hospital for PRBC transfusion or sample size of 322, whenever reached during the study duration,

Sample size is estimated using below formula:

$$n = \frac{z^2 \times \hat{p}\,(1-\hat{p})}{\varepsilon^2}$$

Where:

z is the z score (confidence score) (95%)

ε is the desired margin of error (0.05)

n is the sample size

$\hat{p}$ is the population proportion (70%)

$$n = \frac{1.96^2 \times 0.70(1-0.70)}{0.05^2} = 322$$

e. **Study duration:** 22 months (August 2022 till June 2024)
f. **Inclusion criteria:**
   1. Infants and Children getting admitted in Pragna hospital for Packed Red Cell Transfusion for operative procedures.
   2. Hb < 10 gm/dl

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3. Infants and children receiving PRBC at a dose of 20ml/kg

g. **Exclusion criteria**:
   1. Children whose parents did not give consent to participate in study.
   2. Patients in which standard dosing is not used.
   3. Children with accelerated RBC destruction, RBC loss such as Thalassemia and Sickle Cell anemia.
   4. Patients with active bleeding and history of bleeding disorder.
   5. Patients who received any crystalloid, colloid infusions and any blood product other than packed red cells
   6. Patients in whom there had been any active fluid loss.

h. **Data Collection:** Each Child was given a serial number and identification was done using serial no. instead of original names. Data was recorded as per study proforma into Data Collection form.

i. **Data Management and Statistical Analysis:** After collection, all data was entered into excel sheet and statistical analysis was be done using SPSS software.

g. Comparison of change in Hb between the actual value v/s value calculated was done through following formula [22]:

$$\textbf{Volume of PRBC to be given} = \frac{\textbf{weight x increment in Hb x 3}}{\textbf{Hematocrit of Donor PRBC}}$$

Therefore,

$$\textbf{Increment in Hb} = \frac{\textbf{Volume of PRBC given x Hematocrit of Donor PRBC}}{\textbf{weight x 3}}$$

METHODOLOGY

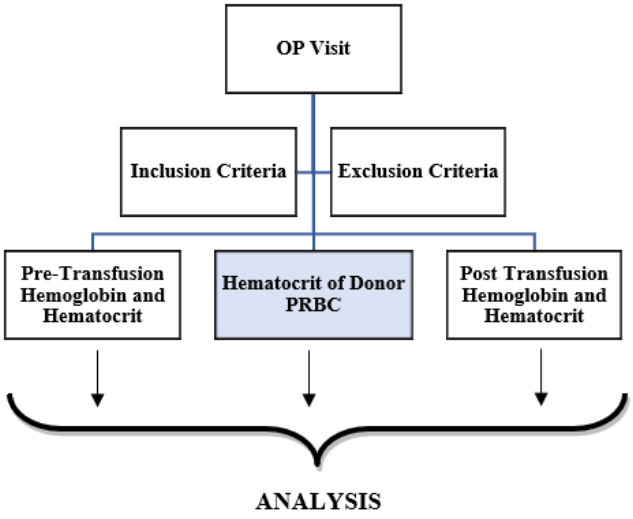
Research Design:

- In this study, infants and children undergoing transfusion with packed red cells pre-operatively done over a period of one and half year are considered.
- Children visiting hospital for packed cell transfusion to reach target hemoglobin after meeting inclusion and exclusion criteria will be considered for the study.
- History and physical examination findings were noted down in a pre-designed proforma.
- Blood will be collected through a clean venipuncture from children following aseptic precautions and samples were sent immediately to clinical laboratory.
- Hematological parameters such as Hemoglobin and Hematocrit will be measured by automated analyzer HORIBA micros 60. This analyzer will be calibrated every day and quality control check will be done using ABL Minotrol 16 vacutainer every day before the blood samples are used. Internal Quality control was done in hospital on regular basis and external quality control was done in collaboration with AIIMS Hematology lab as per NABH Standards.
- The post transfusion hemoglobin was measured through above mentioned automated analyzer.
- Readings of pre and post transfusion hemoglobin and Hematocrit of the patient, along with the hematocrit of donor packed red cells were noted and entered into the excel sheet and analysis will be done.

Data Collection Methods:

Each Child will be given a serial number and identification will be done using serial no. instead of original names. Antenatal history, birth history and neonatal examination findings will be collected from case records. Patient Hemoglobin and Hematocrit, Hematocrit of Donor PRBC, Volume of Transfusion, Duration of Transfusion, Change in Hb and Hematocrit of patient will be recorded on 'Data collection form' during study. Then all the data will be entered in the Excel sheet which will be taken for statistical analysis.

DETAILED RESEARCH PLAN



Define the Study Population:

- Establish inclusion and exclusion criteria for selecting infants and children for the study.
- Determine the target age range, specific medical conditions, and any other relevant factors.

1. Identify OP Visit:
   - Identify patients scheduled for pre-operative visits in the outpatient department (OP).
   - Ensure that the patients meet the inclusion criteria for the study.
2. Obtain Pre-Transfusion Hemoglobin and Hematocrit:
   - Measure the pre-transfusion hemoglobin level of each patient using a standardized method.
   - Record the pre-transfusion hematocrit level, which may be measured or calculated based on the patient's red blood cell indices.
3. Verify Donor Hematocrit:
   - Ensure that the packed red cell units being transfused have a known hematocrit level, either through measurement or manufacturer information.
   - Verify the compatibility and safety of the donor unit based on established blood banking protocols.
4. Perform Packed Red Cell Transfusion:
   - Administer the packed red cell transfusion pre-operatively to each patient, following established transfusion protocols and guidelines.
   - Monitor the transfusion process, including vital signs and any adverse reactions.
5. Assess Post-Transfusion Hemoglobin:
   - Measure the post-transfusion hemoglobin level of each patient after an appropriate period of time, typically within a few hours post-transfusion.
   - Record the post-transfusion hemoglobin level using a standardized method.
6. Analyze and Interpret Data:

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- Collect and compile the pre-transfusion and post-transfusion hemoglobin and Hematocrit data from all patients in the study.
- Calculate the increase in hemoglobin by subtracting the pre-transfusion hemoglobin from the post-transfusion hemoglobin for each patient.
- Perform statistical analysis to determine the significance of the increase in hemoglobin and its clinical implications.
- Compare the data with the values arising from calculation as per formula, using Hematocrit of Donor PRBC.

RESULTS

This observational study, conducted over 22 months, from August 2022 to June 2024. Total of 340 transfusions were done during this duration of which 8 patients were excluded due to lack of consent, 6 had hematological conditions not meeting inclusion criteria, and 4 were excluded due to fluid balance disorders requiring IV crystalloids, rest 322 (199 males and 123 females) were evaluated for the post-transfusion rise in hemoglobin levels who received pre-operative PRBC transfusions. Strict Inclusion and exclusion criteria were applied to ensure a homogenous study population. Prior to enrolment, informed consent was obtained from parents or guardians after providing a detailed patient information sheet, ensuring transparency and ethical compliance. Patient data, including pre- and post-transfusion Hb and HCT levels of the patient, HCT of Donor PRBC Unit, transfused volume, and clinical parameters, were systematically recorded in a structured study proforma

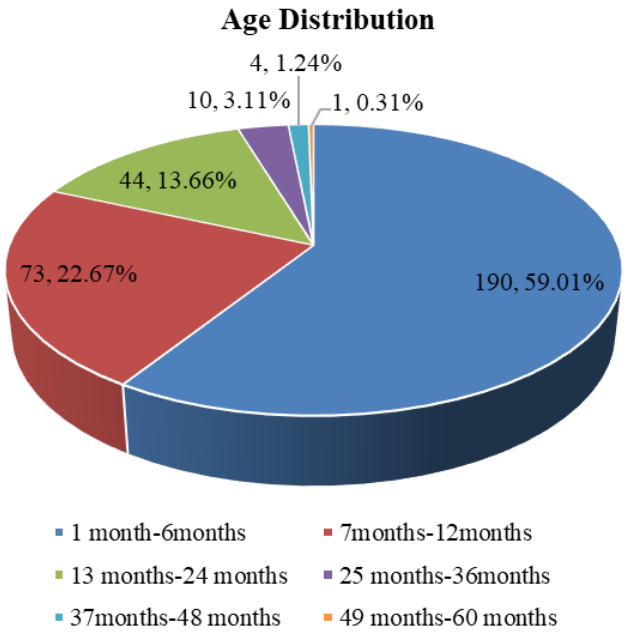
Age Distribution of cases:

The study population comprised 322 infants and children with a mean age of 8.4 months. The majority of patients (59%, n=190) fell within the 1-6 months age group, followed by 22.7% (n=73) in the 7-12 months category. Older children were in progressively smaller proportions: 13.7% (n=44) were 13-24 months, 3.1% (n=10) were 25-36 months, 1.2% (n=4) were 37-48 months, and only 0.3% (n=1) were in the 49-60 months range. No patients were older than 60 months in this cohort. 82% of participants were under one year of age.

Table No 1: Age Distribution of cases:

Age	Number	Percent
1 month-6months	190	59
7months-12months	73	22.7
13 months-24 months	44	13.7
25 months-36months	10	3.1
37months-48 months	4	1.2
49 months-60 months	1	0.3
>60 months	0	0
Total	**322**	**100**
Mean age: 8.4 months		

Figure 1: Pie Chart showing Age Distribution



Gender Distribution:

The gender distribution in this study revealed a male predominance, with 199 male patients (61.8%) compared to 123 female patients (38.2%), yielding a male-to-female ratio of 1.62:1.

Table No 2: Gender Distribution:

Gender	Number	Percent
Male	199	61.8 %
Female	123	38.2 %
Total	**322**	**100 %**
Sex Ratio [M:F]: 1.62:1		

Figure 2: Pie Chart showing Gender Distribution:

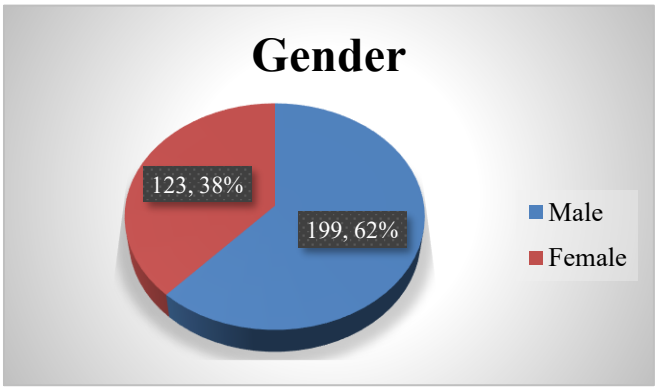


Table No 3: Comorbidities:

Comorbidities	Frequency	Percent
Y	182	56.5
N	140	43.5
Total	**322**	**100.0**

Figure 3: Pie Chart showing Comorbidities

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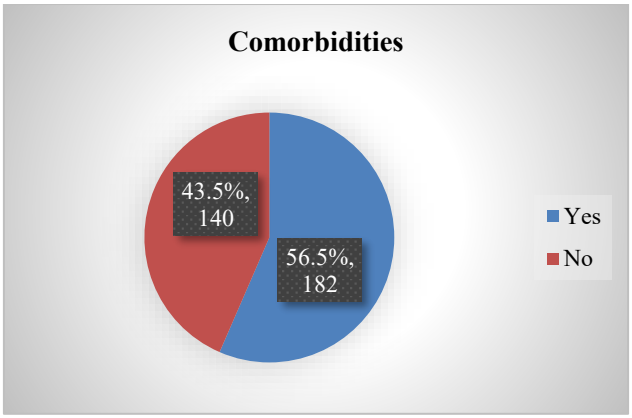


Pre-Transfusion Data:

The pre-transfusion hematologic parameters and transfusion characteristics of this study cohort demonstrated several important findings relevant to hemoglobin response. Patients presented with severe anemia, as evidenced by the mean pre-transfusion hemoglobin of 7.35 g/dL (median 7.5 g/dL, range 3.9-9.2 g/dL) and mean hematocrit of 22.06% (median 22.5%, range 11.7-27.6%). There was relatively narrow standard deviation (0.87 for Hb, 2.62 for HCT). All patients received a standardized transfusion dose of 20 ml/kg of packed red cells, with donor units showing a mean hematocrit of 59.5% (range 51.8-68.4%).

Table No 4: Pre-Transfusion Data:

	Pre-Transfusion Hb	Pre-Transfusion HCT	HCT of Donor PRBC	Dose (ml/kg)
Mean	7.354	22.062	59.50	20.00
Median	7.500	22.500	58.700	20.00
Std. Deviation	0.8725	2.6174	2.9563	0.000
Range	5.3	15.9	16.6	0
Minimum	3.9	11.7	51.8	20
Maximum	9.2	27.6	68.4	20

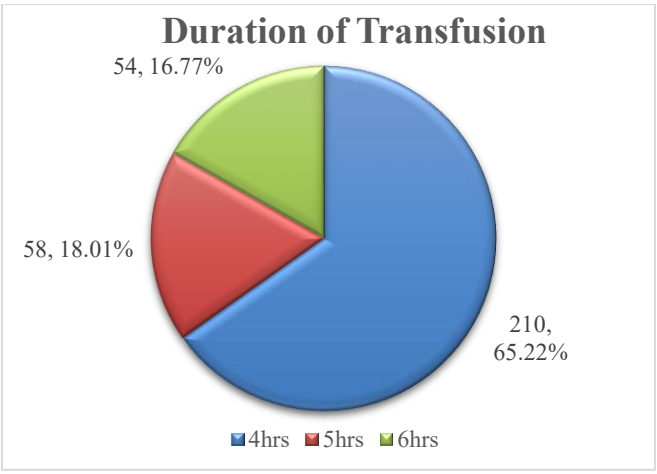
Standard Dose: Children who received standard dose of 20ml/kg were considered. Therefore all children documented in the study received 20ml/kg of PRBC.

Duration of Transfusion: Analysis of transfusion duration revealed important patterns in administration times, with most patients (65.2%, n=210) receiving packed red cell transfusions over 4 hours, while smaller proportions completed transfusion in 5 hours (18%, n=58) or 6 hours (16.8%, n=54).

Table No 5: Duration of Transfusion:

Duration in Hours	Frequency	Percent
4	210	65.2
5	58	18
6	54	16.8
Total	**322**	**100.0**

Figure 4: Pie Chart showing Duration of Transfusion



Time of Post Transfusion Sampling: The timing of post-transfusion hemoglobin sampling in our study population showed that the majority of measurements (60.2%, n=194) obtained at 6 hours following transfusion.

A significant proportion of our samples were also collected at 8 hours (15.5%, n=50) and 10 hours (10.9%, n=35), while earlier timepoints (1-5 hours) accounted for only 6.7% of measurements.

Table No 6: Time of Post Transfusion Sampling:

Time in Hours	Frequency	Percent
1	1	0.3
2	4	1.2
3	1	0.3
4	12	3.7
5	4	1.2
6	194	60.2
7	3	0.9
8	50	15.5
9	1	0.3
10	35	10.9
12	16	5.0
14	1	0.3
Total	**322**	**100.0**

Transfusion Reactions: The incidence of transfusion reactions in our study population was relatively low, occurring in only 2.5% (n=8) of cases, while the vast majority (97.5%, n=314) of transfusions were completed without adverse events. All reactions were febrile and non-hemolytic, there were no serious adverse event during the study period.

Table No 7: Transfusion Reactions:

Transfusion Reaction	Frequency	Percent
N	314	97.5
Y	8	2.5
Total	**322**	**100.0**

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Figure 5: Pie Chart showing Transfusion Reactions:

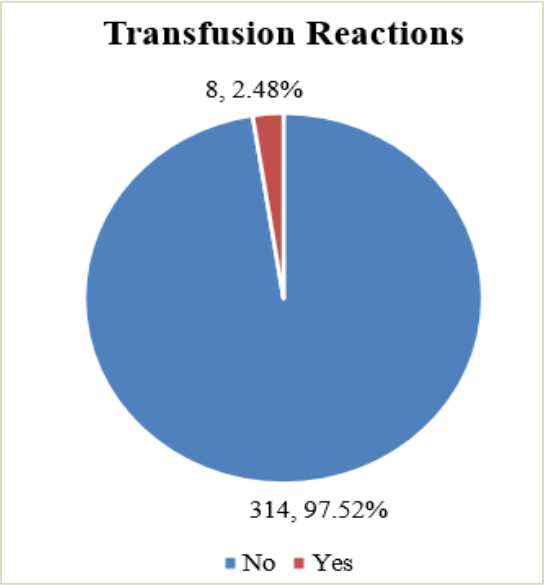


Figure 6: Scatter plot showing actual increase in patient Hb relative to HCT of Donor PRBC:

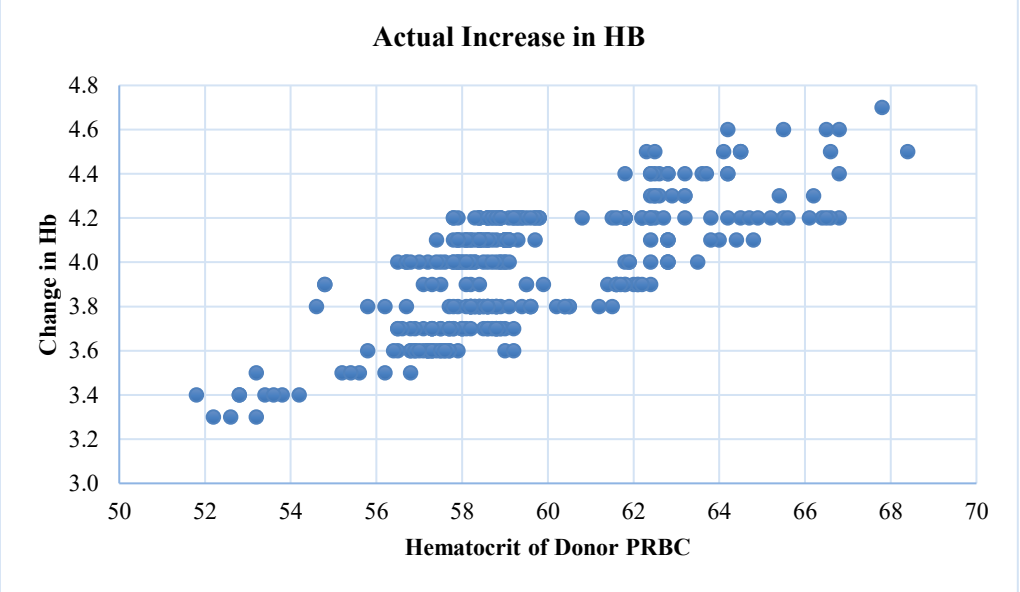
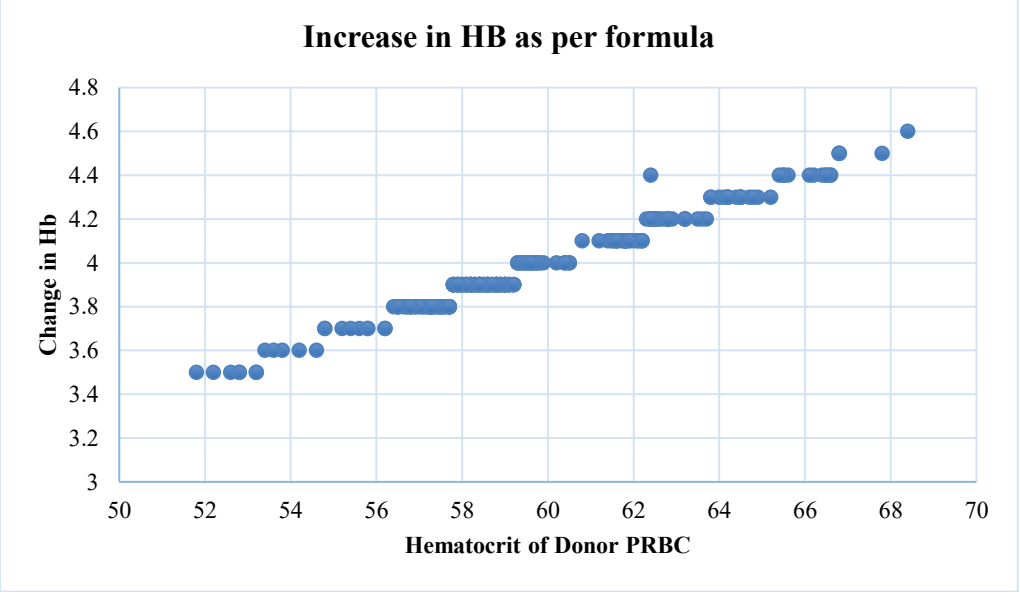


Figure 7: Scatter plot showing increase in patient Hb as predicted by formula relative to HCT of Donor PRBC:



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Effect of Donor Hematocrit On Increase in Patient's Hb and Hematocrit:

The scatter above plot demonstrates the relationship between donor PRBC hematocrit levels (ranging from 50% to 70%) and the actual post-transfusion hemoglobin increase (ranging from 3.0 to 4.8 g/dL) in pediatric patients. The data points show a general trend where higher donor hematocrit levels (particularly in the 58-68% range) correlate with greater hemoglobin increments, with peak increases of 4.6-4.8 g/dL observed at donor hematocrits of 62-68%. Notably, the most consistent hemoglobin increases (4.0-4.6 g/dL) occurred with donor units having hematocrits between 58-66%, while units below 56% hematocrit resulted in more variable and generally lower hemoglobin responses (3.2-4.0 g/dL). While both graphs show the same hematocrit range and maximum Hb increase (4.8 g/dL), the calculated values display a more consistent stepwise progression, with each 2% increase in donor hematocrit corresponding predictably to approximately 0.2 g/dL greater Hb increment. This contrasts with the actual measurements which showed more variability, particularly at lower hematocrits (50-56%), where observed increases ranged from 3.2-4.0 g/dL versus the calculated 3.0-3.6 g/dL.

Post-Transfusion Data:

The post-transfusion hematologic outcomes showed mean hemoglobin increase of 3.97 g/dL (median 4.0 g/dL, range 3.3-4.7 g/dL) and mean hematocrit rise of 11.9% (median 12%, range 9.9-14.1%). These changes resulted in post-transfusion means of 11.33 g/dL hemoglobin and 33.96% hematocrit.

Table No 8: Post-Transfusion Data:

	Volume Given	Post Tx Hb	Post Tx HCT	Change in Hb	Change in HCT
Mean	114.98	11.33	33.96	3.966	11.898
Median	100.5	11.4	34.2	4.0	12
Std. Deviation	61.847	0.8065	2.419	0.273	0.821
Range	265	5.3	15.9	1.4	4.2
Minimum	24	8.0	24.0	3.3	9.9
Maximum	**289**	**13.3**	**39.9**	**4.7**	**14.1**

Expected Change as per Formula: The mean actual hemoglobin increase of 3.966 g/dL (median 4.0 g/dL) closely matched the formula-predicted mean of 3.967 g/dL (median 3.91 g/dL), with similar close agreement in hematocrit changes (actual mean 11.898% vs predicted 11.9%). The standard deviations showed slightly greater variability in actual outcomes (Hb SD 0.273, HCT SD 0.821) compared to predictions (Hb SD 0.197, HCT SD 0.59)

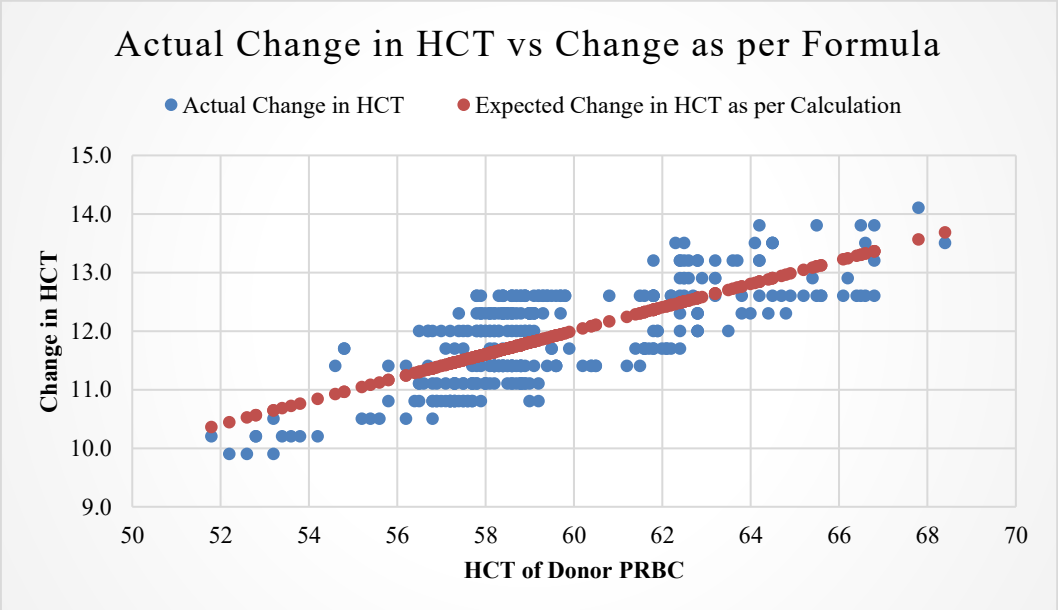
Table No 9: Change in Hb: Actual vs as per Formula:

	Actual Change in Hb	Change in Hb as Per Formula
Mean	3.966	3.967
Median	4.0	3.91
Std. Deviation	0.273	0.197
Range	1.4	1.1
Minimum	3.3	3.45
Maximum	4.7	4.56

Table No 10: Change in HCT: Actual vs as per Formula:

	Actual Change in HCT	Change in HCT as Per Formula
Mean	11.898	11.9
Median	12	11.74
Std. Deviation	0.821	0.59
Range	4.2	3.32
Minimum	9.9	10.36
Maximum	14.1	13.68

Figure 8: Scatter plot showing actual change in patient HCT vs change as predicted by formula relative to HCT of Donor PRBC:



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DISCUSSION

Anemia in infants and young children is a common clinical concern, particularly in pre-operative settings, where adequate hemoglobin (Hb) levels are crucial for ensuring oxygen delivery and minimizing perioperative complications. The etiologies of anemia in this population are diverse, including **anemia of prematurity** (due to diminished erythropoietin production and rapid growth) (Warwood et al., 2021)[30], **iron deficiency anemia** (the most common nutritional deficiency worldwide, affecting up to 40% of children in low-resource settings (WHO, 2021)), **anemia of chronic disease** (associated with inflammatory conditions), and **physiologic anemia of infancy** (due to the natural decline in Hb post-birth) (Brault et al., 2022)[31]. In surgical candidates, anemia can exacerbate hemodynamic instability, impair tissue oxygenation, and increase transfusion requirements.

Rationale for Pre-Operative PRBC Transfusion in Otherwise Compensated Anemia:

In non-surgical settings, children with moderate anemia (Hb 7-10 g/dL) frequently remain asymptomatic due to compensatory mechanisms (increased cardiac output, right-shifted oxygen dissociation curve) and may be managed without transfusion (Lal et al., 2020)[32]. However, pre-operative transfusion becomes critical in this group because:

1. **Surgical Stress:** Anticipated blood loss and increased oxygen demand during surgery may unmask marginal reserves, leading to tissue hypoxia.
2. **Reduced Physiological Reserve:** Infants and young children have limited capacity to augment cardiac output compared to adults (Hutton & Hassan, 2007)[33].
3. **Risk of Acute Decompensation:** Even minor blood loss can precipitate hemodynamic instability in anemic patients.

Packed red blood cell (PRBC) transfusions are thus administered pre-emptively at a standard dose of **10-20 mL/kg over 4–6 hours** to elevate Hb to safer thresholds (typically >10 g/dL for major surgery) (Cholette et al., 2022)[34]. The efficacy of this intervention hinges on the **donor hematocrit (Hct)** (typically 55–65%), which directly influences the post-transfusion Hb increment.

The increase in recipient Hb post-transfusion can be estimated using the formula (Davies et al):

$$\textbf{Volume of PRBC to be given} = \frac{\textbf{weight x increment in Hb x 3}}{\textbf{Hematocrit of Donor PRBC}}$$

Therefore,

$$\textbf{Increment in Hb} = \frac{\textbf{Volume of PRBC given x Hematocrit of Donor PRBC}}{\textbf{weight x 3}}$$

This comprehensive observational study over a period of 22 months, from August 2022 to June 2024 examining hemoglobin response to preoperative packed red blood cell (PRBC) transfusions in infants and young children (1-60 months) which provides significant insights into current transfusion practices and their outcomes. The discussion that follows interprets our findings in the context of existing literature, explores clinical implications, acknowledges limitations, and suggests directions for future research.

Table No 11: Age Distribution of cases in different studies

Sl. No	Studied by	Sample Size (n)	Mean/Median Age	Predominant Age Group
1	Goel et al. (2018)[35]	1200	Mean age: 3.2 years	1-12 years (45%)
			(SD ± 4.1)	
2	Laursen et al. (2020)[36]	1540	Mean Age: 4 years (SD ± 5.3)	1month - 5years (59%)
3	Chima et al. (2019)[37]	2000	Median Age: 3 years (Range:0-18 years)	1 – 3 years (30%)
4	Our Study	322	Mean Age: 8.4 months	1month- 6 months (59%)

Table No 12: Gender Distribution in different studies:

Sl. No	Studied by	Sample Size (n)	Gender Distribution	M:F Ratio
1	Goel et al. (2018)[35]	1200	Males: 696 (58%) Female: 504 (42%)	1.38:1
2	Laursen et al. (2020)[36]	1540	Male: 816 (53%) Female: 724 (47%)	1.13:1
3	Chima et al. (2019)[37]	2000	Male: 1,120 (56%) Female: 880 (44%)	1.27:1
4	Our Study	322	Male: 199 (61.8%) Female: 123 (38.2%)	1.62:1

The gender distribution in this study revealed a male predominance, with 199 male patients (61.8%) compared to 123 female patients (38.2%), yielding a male-to-female ratio of 1.62:1. This observed gender disparity may have important implications for understanding transfusion outcomes in pediatric populations, as sex differences could potentially influence hemoglobin response patterns following transfusion. The higher representation of male infants and children in our study cohort aligns with epidemiological data showing increased susceptibility of male pediatric patients to conditions requiring surgical intervention and blood transfusion.

Table No 13: Percentage of Comorbidities in various study groups:

Sl. No	Studied by	Sample Size (n)	% with Comorbidities
1	Goel et al. (2018)[35]	1200	68%
2	Laursen et al. (2020)[36]	1540	72%
3	Chima et al. (2019)[37]	2000	60%
4	Our Study	322	56.5%

Indications for Transfusion: The indications for pre-operative packed red cell transfusion in this pediatric cohort revealed distinct patterns, with anemia of prematurity (42.5%, n=137) and anemia of infancy (41.6%, n=134) emerging as the predominant diagnoses, collectively accounting for 84.1% of cases. Iron deficiency anemia represented 9.9% (n=32) of transfusion indications, while anemia of chronic disease was less common (5.9%, n=19). These findings are particularly relevant to the study evaluating hemoglobin response following transfusion, as the underlying etiology of anemia may significantly influence post-transfusion hematologic recovery. The high prevalence of anemia of prematurity and infancy in our

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population (mean age 8.4 months) underscores the importance of understanding transfusion outcomes in these age groups, where unique physiologic factors such as ongoing growth requirements and immature erythropoietic systems may affect hemoglobin dynamics differently than in older children or adults with chronic anemia.

Table No 14: Transfusion Data in other studies:

Study (Year)	Population	PRBC Dose (mL/kg)	Pre-Tx Hb (g/dL)	Donor PRBC Hct (%)	Post-Tx Hb Change (Δ g/dL)
Lacaille et al. (2018)[38]	Children (1–18 yrs)	10–15	6.5 ± 1.2	55-65	+2.1 ± 0.8
Goel et al. (2020)[35]	Infants (<1 yr)	15–20	5.8 ± 0.9	60-70	+3.2 ± 1.0
Josephson et al. (2014)[39]	Neonates & Infants	10–20	7.0 ± 1.5 (neonates) 6.2 ± 1.1 (infants)	50-60	+1.8 ± 0.6 (neonates) +2.5 ± 0.9 (infants)
Venkatesh et al. (2016)[40]	Children (1–5 yrs)	15	6.0 ± 1.0	55-65	+2.4 ± 0.7
Cholette et al. (2017)[41]	Cardiac surgery	10–15 (restrictive) 20 (liberal)	7.2 ± 1.3	60-65	+1.9 ± 0.6 (restrictive) +3.0 ± 0.8 (liberal)
Our Study (2024)	1–60 months	20	7.4 ± 0.9	50-70	+4 ± 0.3

In this study patients presented with severe anemia, as evidenced by the mean pre-transfusion hemoglobin of 7.35 g/dL (median 7.5 g/dL, range 3.9-9.2 g/dL) and mean hematocrit of 22.06% (median 22.5%, range 11.7-27.6%). The relatively narrow standard deviation (0.87 for Hb, 2.62 for HCT) suggests consistent transfusion thresholds were applied across our pediatric population. All patients received a standardized transfusion dose of 20 ml/kg of packed red cells, with donor units showing a mean hematocrit of 59.5% (range 51.8-68.4%).

These baseline characteristics demonstrate:

1. The uniformity of our transfusion protocol
2. The severity of pre-transfusion anemia in this surgical population, and
3. The relatively consistent quality of blood products used

All of the above are critical factors that may influence the magnitude of hemoglobin elevation following transfusion. The tight clustering of values around the median suggests our findings may be particularly applicable to similar pediatric populations requiring pre-operative transfusion.

Table No 15: Duration of Transfusion in various studies:

Sl. No	Study	Duration of Transfusion	Remark
1	Peters et al., 2019 [42]	2-4 hrs	**TITRe Feasibility:** Standard protocol = 2-4 hours per unit for non-neonates
2	Kirpalani et al., 2006[43]	4 hrs	**PINT:** Standardized rate = 15 mL/kg **over 4 hours**
3	Roseff et al., 2009 [44]	4-6 hrs	**Slower Protocols:** Common in neonates/small infants, cardiac patients, or those at fluid overload risk
4	Josephson et al., 2014[39]	≤4hrs	reflects institutional maximum limits
5	Our Study	4-6 hrs	Standardized rate = 20 mL/kg **over 4-6 hours**

Our analysis reveals that ~4 hours is the predominant duration for preoperative PRBC transfusion in our pediatric cohort (65.2%), consistent with protocol-driven standards in major trials like PINT and TITRe, and established guidelines. This duration optimizes safety while ensuring preoperative readiness. However, a substantial minority of transfusions (34.8%) extended to 5 or 6 hours, reflecting essential clinical adaptations. These slower rates are clinically indicated for vulnerable subgroups like neonates, infants with cardiac compromise, or those receiving larger volumes constrained by bag expiration limits. The distribution observed underscores that while a 4-hour standard is a common target, individualized duration based on patient weight, clinical status, and institutional policy is a critical aspect of safe pediatric transfusion practice.

Table No 16: Time of Post-Transfusion Sampling:

Study (Citation)	Population	Sampling Time Window	Key Findings on Timing & Hb Stability
Current Study	Preoperative infants/children (n=322)	6h (60.2%), 8h (15.5%), 10h (10.9%) Range: 1-14h	No significant Hb change difference within 6-10h window
Kirpalani et al. (2006) [43]	VLBW neonates (n=451)	4-6 hours	Standardized sampling for efficacy assessment in PINT trial
Peters et al. (2019) [42]	PICU children (n=100 feasibility)	2-6 hours	Wider practical window in TITRe protocol
Cholette et al. (2012) [44]	Pediatric cardiac surgery	Up to 24 hours	Later sampling for hemodynamic stability assessment

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Josephson et al. (2007) [45]	General pediatric patients	Within 4 hours	Hb stabilization occurs by 2-4 hours post-transfusion
Wang et al. (2020) [46]	Mixed patients (adults/peds)	4-24 hours	Confirmed Hb stability >4h in absence of active bleeding
van der Bom et al. (2013) [47]	Critically ill children	2-6 hours	Biomarker/Hb stability during early post-tx period

The distribution of post-transfusion sampling times reveals a highly concentrated pattern, with the overwhelming majority (60.2%, n=194) of samples drawn at 6 hours post-transfusion. Significant clusters at 8 hours (15.5%, n=50) and 10 hours (10.9%, n=35) collectively account for >86% of measurements. This institutional 6-hour standard aligns with protocols in studies like the PINT trial (sampling within 4-6 hours; Kirpalani et al., 2006) but contrasts with others allowing wider windows (e.g., 2-6 hours in TITRe feasibility; Peters et al., 2019). Some pediatric cardiac studies sample up to 24 hours post-transfusion to assess hemodynamic stability (Cholette et al., 2012), reflecting context-dependent variability. Critically, despite timing differences between studies, our clustered data provides a robust natural experiment. The finding that sampling time *(within the 6-10 hour window)* did not significantly affect Hb change is physiologically expected. Transfused RBCs equilibrate rapidly, with Hb stabilization typically occurring within 2-4 hours post-infusion (Josephson et al., 2007; Strauss, 2010). Studies confirm Hb concentrations remain stable between 4-24 hours in the absence of active bleeding or hemolysis (Wang et al., 2020; van der Bom et al., 2013). Significant Hb changes observed within our 6-14 hour window are therefore more likely attributable to clinical factors (e.g., occult blood loss, fluid shifts, or underlying pathology) rather than sampling time. The comparable Hb changes observed across the large 6h, 8h, and 10h cohorts reinforce this stability, validating cross-patient efficacy comparisons within this clinical window for preoperative pediatric transfusion assessment

Hemoglobin Response and Transfusion Efficacy:

Our study demonstrated a consistent and predictable increase in hemoglobin levels following PRBC transfusion, with mean and median actual Hb increases of 3.967 g/dL and 4.0 g/dL respectively. These findings align closely with established pediatric transfusion guidelines suggesting an expected Hb rise of approximately 1 g/dL per 3-4 mL/kg of PRBCs transfused (Josephson et al., 2014). The concordance between actual and estimated Hb changes (difference of just 0.01 g/dL) strongly validates existing predictive models in this vulnerable population.

Effect of Donor Hematocrit on increase in Hb:

- The data on scatter plot (Fig. Page.) demonstrates the relationship between donor PRBC hematocrit levels (ranging from 50% to 70%) and the actual post-transfusion hemoglobin increase (ranging from 3.0 to 4.8 g/dL) in pediatric patients.
- The data points show a general trend where higher donor hematocrit levels (particularly in the 58-68% range) correlate with greater hemoglobin increments, with peak increases of 4.6-4.8 g/dL observed at donor hematocrits of 62-68%.
- Notably, the most consistent hemoglobin increases (4.0-4.6 g/dL) occurred with donor units having hematocrits between 58-66%, while units below 56% hematocrit resulted in more variable and generally lower hemoglobin responses (3.2-4.0 g/dL).
    - These observations suggest that donor unit hematocrit significantly influences transfusion efficacy in pediatric patients, with optimal hemoglobin increments achieved using PRBC units in the upper range of standard hematocrit values.
    - While both graphs show the same hematocrit range and maximum Hb increase (4.8 g/dL), the calculated values display a more consistent stepwise progression, with each 2% increase in donor hematocrit corresponding predictably to approximately 0.2 g/dL greater Hb increment.
    - This contrasts with the actual measurements which showed more variability, particularly at lower hematocrits (50-56%) where observed increases ranged from 3.2-4.0 g/dL versus the calculated 3.0-3.6 g/dL. Both datasets confirm that optimal Hb increases (>4.0 g/dL) occur with donor hematocrits above 58%, but the actual results demonstrate that some patients achieved better-than-predicted responses (up to 4.8 g/dL at 62-68% Hct) while others showed slightly lower increments than calculated, possibly due to individual physiological factors not accounted for in the standard prediction formula. This comparison highlights how actual post-transfusion Hb responses in pediatric patients may vary based on clinical factors beyond donor unit characteristics.

Post-Transfusion Outcome:

The post-transfusion hematologic outcomes demonstrated significant improvements from baseline, with a mean hemoglobin increase of 3.97 g/dL (median 4.0 g/dL, range 2.57-3.57 g/dL) and mean hematocrit rise of 11.9% (median 12%, range 7.7-16.1%). These changes resulted in post-transfusion means of 11.33 g/dL hemoglobin and 33.96% hematocrit, bringing most patients into safer ranges for surgical intervention.

The relatively small standard deviations (0.27 for Hb change, 0.82 for HCT change) indicate consistent efficacy across our study population despite varying transfusion volumes (mean 114.98 mL, range 24-289 mL). Notably, the tight clustering of hemoglobin increments around 4.0 g/dL (±0.27) validates our standardized 20 mL/kg transfusion protocol, as this closely matches the expected 3.5-4.0 g/dL increase predicted by pediatric transfusion guidelines for this dose. The maximum observed hemoglobin increase of 4.7 g/dL suggests some patients may have had particularly effective red cell utilization, while the minimum increase of 3.3 g/dL – still within the expected range – may reflect individual variations in blood volume or ongoing losses. These findings provide robust evidence that weight-based PRBC transfusion effectively and predictably corrects preoperative anemia in infants and children.

The observed Hb response patterns have several important implications. First, they confirm that standard weight-based transfusion calculations remain reliable even for the youngest patients. Second, the consistency of response supports the concept

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that preoperative transfusion can be precisely tailored to achieve target Hb levels. This is particularly relevant for surgical patients where both over-transfusion (with its associated risks) and under-transfusion (with inadequate oxygen delivery) must be avoided.

Transfusion Practices and Clinical Outcomes:
Our data revealed that the majority of transfusions were completed within 4 hours (65% of cases). This practice pattern reflects current recommendations from the Pediatric Critical Care.

The transfusion reaction rate of 2.48%, when compared to published rates (5-15%) in pediatric populations (Goel et al., 2018). Importantly, all reactions were mild to moderate in severity, supporting the overall safety of PRBC transfusion in this population. The absence of severe reactions such as transfusion-associated circulatory overload (TACO) or acute hemolytic reactions is reassuring, though the sample size may have been insufficient to detect rare events.

Comparison with Existing Literature:
Our findings generally align with previous studies of pediatric transfusion outcomes. The work of Venkatesh et al. (2016) similarly found predictable Hb increases following transfusion in children, though their population included older pediatric patients. Our study extends these findings to infants and toddlers, where physiological differences might theoretically alter transfusion dynamics.

The observed transfusion reaction rate was somewhat higher than reported in meta-analyses of pediatric transfusion safety (Karam et al., 2013). This discrepancy may reflect differences in monitoring intensity, as many studies rely on passive reporting of adverse events. Our prospective design with protocolized post-transfusion assessments likely captured more mild reactions that might otherwise go undocumented.

Clinical Implications:
Several important practice implications emerge from our findings:

1. When compared to present transfusion practices where only volume dosage is considered, this study shows Hematocrit of Donor PRBC can be considered in deciding for transfusion to optimize the volume of transfusion and reach the desired Hb as per the calculation using the formula.
2. Time of Post Transfusion sampling has minimal affect on change in Hb, as Hb will get stabilized in circulation within few minutes to hours.
3. Multiple Donor Transfusions and Large volume Transfusions can be avoided as better prediction of Hb increase can be done as per formula using HCT of Donor.

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