CASE REPORT

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Packed red cell transfusions in preterm neonates: a retrospective study

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ABSTRACT

Introduction: Preterm neonates are highly vulnerable to anemia. Packed red cell (PRC) transfusions are often necessary but must be carefully considered due to associated risks. This study aims to assess the characteristics of preterm infants who received PRC transfusions to guide safer and effective transfusion practices.

Methods: This study was conducted using a retrospective descriptive approach. It included preterm neonates who received PRC transfusions, as documented in the medical records from July 2022 to March 2025. Patient characteristics, hemoglobin level, transfusion profile, and comorbidities in preterm neonates receiving PRC transfusions were evaluated.

Results: The sample consisted of 52 neonates, 37 boys, and 15 girls. The gestational age of infants was mainly between 28 and <32 weeks (64,5%). Most neonates were very low birth weight, which is 53,8%. The mode of delivery was relatively similar between spontaneously and cesarean section. The average length of hospital stay was 35.27 ± 16.62 days. The initial hemoglobin level of preterm infants receiving PRC transfusions averaged 10.88 ± 1.33 g/dL. The first transfusion was typically administered at 18.10 ± 9.69 days of life. Notably, most infants (59.6%) required three or fewer transfusions. The most common comorbidity among preterm infants receiving PRC transfusions was respiratory distress syndrome (RDS) at 78.8%, followed by neonatal jaundice (53.8%) and asphyxia (40.4%). Most RDS cases (69.2%) were caused by hyaline membrane disease (HMD).

Conclusion: Preterm neonates receiving PRC transfusions had a high-risk profile, underscoring the importance of individualized transfusion thresholds and close post-transfusion monitoring to improve clinical outcomes.

Keywords: hyaline membrane disease, preterm neonates, red cell transfusion, respiratory distress syndrome.
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INTRODUCTION

Premature birth, as defined by the World Health Organization (WHO), refers to infants born before 37 completed weeks of gestation. Preterm birth is associated with a wide array of complications, both immediate and long-term, one of which is anemia of prematurity (AOP). AOP is a common condition in preterm neonates and is characterized by a significant decline in hemoglobin levels, which occurs more rapidly and severely compared to term infants. While full-term infants typically experience a mild, often asymptomatic drop in hemoglobin levels, preterm infants face more pronounced anemia, which may require medical intervention. The underlying causes of AOP are multifactorial, including immaturity of the hematopoietic system, reduced erythropoietin (EPO) production, shorter red blood cell lifespan, and frequent blood sampling. These factors make preterm neonates particularly vulnerable to the early onset of anemia, which can compromise oxygen delivery and affect their overall development.[1–3]

Anemia of prematurity (AOP) is particularly prevalent in extremely low birth weight (ELBW) infants, with up to 80% of these infants requiring packed red cell (PRC) transfusions to manage the condition.[4] AOP arises due to a combination of several contributing factors, including diminished erythropoietin (EPO) production, a shorter lifespan of red blood cells, frequent blood sampling that depletes blood volume, and inadequate nutrition, all of which are common in preterm infants. The hematopoietic system in preterm infants is often underdeveloped, leading to an impaired ability to produce and sustain sufficient red blood cells. As a result, these infants are more likely to experience significant anemia during their early weeks of life. Global data indicate that the prevalence of anemia among preterm infants varies widely, affecting between 6% and 70% of such infants, with the highest burden observed in low- and middle-income countries.[4,5] In these regions, limited access to adequate neonatal care and nutrition, as well as differences in healthcare infrastructure, exacerbate the incidence of AOP, highlighting the need for targeted interventions and better resource allocation in these settings.

PRC transfusion remains the primary treatment for moderate to severe anemia in preterm infants, especially in ELBW neonates. It is typically administered to improve oxygen delivery, support

growth, and prevent complications. However, transfusion practices, including hemoglobin thresholds and clinical indications, vary widely across institutions, reflecting the absence of universally accepted guidelines.[6] Moreover, while transfusions are often life-saving, they are not without risks. Studies have linked PRC transfusions to increased incidence of complications such as necrotizing enterocolitis (NEC), intraventricular hemorrhage (IVH), bronchopulmonary dysplasia (BPD), and retinopathy of prematurity (ROP), and some evidence suggests that higher transfusion exposure does not always translate into improved outcomes.[7,8]

Given these concerns, reducing unnecessary transfusions is a clinical priority. To achieve this, a better understanding of the clinical characteristics and comorbidities of preterm neonates receiving transfusions is essential. Identifying the factors associated with transfusion needs may help guide more individualized and restrictive transfusion strategies that minimize risk while maintaining safety. Therefore, this study aimed to describe the clinical characteristics and comorbidities of preterm neonates with anemia who received packed red cell transfusions during hospitalization. This study is particularly valuable in the Indonesian context, where research on PRC transfusions in preterm neonates is scarce. It adds to the current body of knowledge by providing local insights into transfusion practices and the clinical profiles of preterm infants in Indonesia. By identifying the specific comorbidities and clinical factors that influence transfusion needs, this research may help optimize transfusion protocols in Indonesian neonatal care units, offering a more tailored approach that balances benefits and risks, ultimately improving patient outcomes.

METHODS

Study Design and Setting

This study was a retrospective observational study conducted in the Perinatology and Neonatal Intensive Care Unit (NICU) of Wangaya Regional Hospital, a tertiary referral center in Denpasar, Bali. It analyzed medical records of preterm neonates who received PRC transfusions between June 2022 and March 2025. Data collection was carried out from August to September 2025.

Study Population

All preterm neonates admitted to the Perinatology Unit and NICU during the study period were screened for eligibility. Patients were included if they were born at a gestational age of less than 37 weeks, received PRC transfusions during hospitalization, and had complete medical records available for review. Neonates were excluded if their medical records were incomplete or if they had significant congenital anomalies that could interfere with the clinical course or transfusion practices. A total sampling method was used, and all eligible cases within the period of June 2022 to March 2025 were included in the analysis.

Data Collection

Demographic and clinical data were extracted from patient medical records, including sex, gestational age, birth weight, mode of delivery, and length of hospital stay. Clinical and laboratory data related to anemia and transfusion were also collected, such as initial hemoglobin level prior to the first PRC transfusion, age at first transfusion, and total number of transfusions received during hospitalization. Additionally, data on comorbidities were recorded, including respiratory distress syndrome (RDS), sepsis, hyperbilirubinemia, NEC, apnea of prematurity, and other relevant neonatal conditions.

Statistical Analysis

All statistical analyses were performed using IBM SPSS version 24.0 (IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed using the Kolmogorov–Smirnov test. Continuous data were presented as mean ± standard deviation (SD) for normally distributed variables, or as median with minimum and maximum values for non-normally distributed variables. Categorical data were expressed as frequencies and percentages.

RESULTS

Patient Characteristics

A total of 52 preterm neonates who received PRC transfusions were included in this study. The mean gestational age at birth was 30.0 ± 2.46 weeks, with the majority born between 28 and <32 weeks of gestation (65.4%). Most neonates were male (71.2%), and the mean birth weight was 1384 ± 466.12 grams. The most common birth weight category was 1000–1499 grams (53.8%). Regarding the mode of delivery, 53.8% of neonates were delivered via cesarean section, while 46.2% were born through spontaneous vaginal delivery. The mean length of hospital stay was 35.27 ± 16.62 days (**Table 1**).

Hemoglobin Levels and Transfusion Profile

The mean initial hemoglobin level prior to the first PRC transfusion was 10.88 ± 1.33 g/dL. The mean age at the time of the first transfusion was 18.10 ± 9.69 days. During hospitalization, the mean number of PRC transfusions administered was 3.00 ± 2.62 times per patient. When categorized by transfusion frequency, 59.6% of neonates received ≤3 transfusions, while the remaining 40.4% received more than 3 transfusions (**Table 2**).

Comorbidities in Preterm Neonates Receiving PRC Transfusions

Several comorbid conditions were observed among the preterm neonates who received PRC transfusions (**Table 3**). The most common comorbidity was RDS, present in 78.8% of patients, followed by hyaline membrane disease (69.2%), neonatal jaundice (53.8%), and neonatal sepsis (42.3%). Other frequently encountered conditions included apnea of prematurity (28.8%), asphyxia (moderate: 15.4%, severe: 25.0%), and necrotizing enterocolitis (19.2%). Metabolic and electrolyte disturbances such as hypoglycemia (13.5%), cholestasis (13.5%), hypoalbuminemia (7.7%), hyponatremia (7.7%), and hypokalemia (3.8%) were also documented. Less common findings included pneumonia (9.6%), bronchopulmonary dysplasia (5.8%), and undescended testis (5.8%).

DISCUSSION

This study provides an overview of the clinical characteristics, transfusion profiles, and comorbidities among preterm neonates who received packed red cell (PRC) transfusions during hospitalization. Most neonates were male, born at a mean gestational age of 30 weeks and an average birth weight of 1384 ± 466 g, with more than 65% delivered between 28–32 weeks. These findings align with previous studies showing that lower gestational age and birth weight are strong predictors of transfusion requirements and prolonged hospitalization.[9–12]

The mean initial hemoglobin level before the first transfusion was 10.88 ± 1.33 g/dL, and transfusions were typically initiated around the 18th day of life, with most infants receiving three or fewer transfusions. These results are consistent with previous reports, including those by Fontana et al. (2020) and Franz et al. (2020), which also documented early transfusion needs in preterm neonates.[10–12] However, other studies, such as Wang et al. (2017) and Skubisz et al. (2024), demonstrated higher baseline hemoglobin levels yet greater transfusion frequency in extremely premature infants, highlighting how gestational immaturity accelerates hemoglobin decline.[10,13] Collectively, evidence from the ETTNO and TOP trials supports the use of restrictive, clinically guided transfusion strategies, emphasizing individualized decisions rather than rigid numerical thresholds.[9,11]

Comorbidities such as respiratory distress syndrome (78.8%), hyaline membrane disease (69.2%), neonatal jaundice (53.8%), and neonatal sepsis (42.3%) were the most frequent findings. These complications commonly coexist with anemia and have been similarly reported by Fontana et al. (2020) and Skubisz et al. (2024).[12,13] The presence of sepsis, NEC, BPD, IVH, and metabolic disturbances substantially increases transfusion needs and prolongs hospitalization. Understanding these comorbidities is essential for refining transfusion criteria and improving clinical outcomes.

Anemia in preterm neonates arises from the combined effects of low erythropoietin (EPO) production,

Table 1. Characteristics of preterm neonates receiving PRC transfusions

Characteristics	Transfusion (*n*=52)
Gender, n (%)	
Boys	37 (71.2)
Girls	15 (28.8)
Gestational Age (weeks)	30 ± 2.46
Gestational categories, n (%)	
<28 weeks	3 (5.8)
28-<32 weeks	34 (65.4)
32-36 weeks	15 (28.8)
Birth weight (gram)	1384 ± 466.12
Birth weight categories, n (%)	
<1000 gram	5 (9.6)
1000-1499 gram	28 (53.8)
1500-1999 gram	11 (21.2)
2000-2499 gram	6 (11.5)
≥2500 gram	2 (3.8)
Mode of delivery, n (%)	
Spontaneous delivery	24 (46.2)
Sectio caesarean	28 (53.8)
Length of stays (days)	35.27 ± 16.62

Table 2. Hemoglobin levels and transfusion profile

Characteristics	Transfusion(n=52)
Initial hemoglobin level (g/dL)	10.88 ± 1.33
Age at first transfusion (days)	18.10 ± 9.69
Frequency of transfusion	3.00 ± 2.62
Frequency of transfusion categories, n (%)	
≤3 times	31 (59.6)
>3 times	21 (40.4)

Table 3. Comorbidities in preterm neonates receiving PRC transfusions.

Comorbidities	Transfusion(*n*=52)
Respiratory Distress Syndrome, n (%)	41 (78.8)
Pneumonia	5 (9.6)
HMD	36 (69.2)
Neonatal asphyxia, n (%)	
Moderate	8 (15.4)
Severe	13 (25.0)
Hypoglycemia, n (%)	7 (13.5)
Septic neonatorum, n (%)	22(42.3)
Cholestasis, n (%)	7 (13.5)
Necrotizing Enterocolitis, n (%)	10(19.2)
Icterus Neonatorum, n (%)	28(53.8)
Apnea of prematurity, n (%)	15(28.8)
Bronchopulmonary Dysplasia, n (%)	3(5.8)
Undescended testis, n (%)	3(5.8)
Hypoalbuminemia, n (%)	4(7.7)
Hyponatremia, n (%)	4(7.7)
Hypokalemia, n (%)	2(3.8)

shortened red blood cell lifespan, and frequent phlebotomy. Hepatic immaturity limits EPO response, while inflammation, oxidative stress, and infection further suppress erythropoiesis.[7,14,15] Because of this multifactorial nature, optimizing anemia management requires more than transfusion alone. Restrictive protocols supported by recent trials.[9,11] reduce transfusion exposure without adverse impact, while complementary measures, such as delayed cord clamping, minimal blood sampling, adequate nutrition, iron supplementation, and recombinant human EPO, can help sustain hemoglobin levels and minimize transfusion dependency.[8,16,17]

This study has several limitations. It was a single-center, descriptive study, which may limit the generalizability of its findings. The absence of a non-transfused comparison group prevents causal inference regarding the impact of transfusion on outcomes. Additionally, potential confounders such as disease severity and nutritional status were not adjusted for. Further multicenter, prospective research is warranted to validate these findings across diverse neonatal care settings in Indonesia. Such studies should aim to identify predictive factors for transfusion needs and evaluate the safety and cost-effectiveness of restrictive transfusion thresholds, thereby contributing to the development of national, evidence-based transfusion protocols for preterm neonates.

CONCLUSION

This study highlights the clinical characteristics and comorbidities of preterm neonates with anemia who received PRC transfusions, emphasizing the high burden of anemia in neonates with lower gestational age and birth weight. The findings support the adoption of restrictive transfusion strategies based on clinical condition rather than fixed hemoglobin thresholds. Close monitoring of comorbidities like respiratory distress and sepsis is crucial for guiding transfusion decisions and improving outcomes. This research provides valuable baseline data to inform more individualized, evidence-based transfusion protocols for this high-risk population.

DISCLOSURES

ETHICAL CONSIDERATION

Ethical approval for this study was obtained (No: 000.9.2/5183/RSUDW). All patient data were anonymized and handled with strict confidentiality in accordance with the ethical standards outlined in the Declaration of Helsinki.

FUNDING

This study received no external funding.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

I.C.S. conceived the study, developed the methodology, performed data analysis, and wrote the original draft. D.R. contributed to data collection, analysis, and reviewed & edited the manuscript. P.S.S. and I.W.B.S. supervised the study, contributed to the methodology, and reviewed & edited the manuscript.

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