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Transfusion Medicine in Preterm Infants: Balancing Risks, Benefits, and Future Directions

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Abstract

Preterm infants frequently require blood transfusions due to anemia of prematurity, thrombocytopenia, coagulopathy, and the cumulative effects of phlebotomy losses. Although transfusions remain lifesaving in the neonatal intensive care unit, their use is complicated by evolving evidence, physiological vulnerability, and concerns about both short- and long-term outcomes. Recent randomized trials have clarified the safety of restrictive transfusion thresholds for red blood cells and platelets, yet substantial variation in practice persists globally. Transfusion-associated risks—including necrotizing enterocolitis, pulmonary complications, hemodynamic instability, and immunologic reactions—must be weighed against the benefits of maintaining adequate oxygen delivery and hemostasis in immature infants. Emerging innovations such as neonatal-specific blood components, pathogen-reduced products, bedside monitoring technologies, and biomarker-guided transfusion strategies are reshaping the future of neonatal transfusion medicine. This narrative review synthesizes current evidence on the indications, benefits, and risks of transfusion in preterm infants and outlines future directions aimed at improving safety, individualizing care, and optimizing neurodevelopmental outcomes.

Introduction

Preterm birth remains a major global health challenge, accounting for more than 15 million births annually and contributing significantly to neonatal morbidity and mortality. Advances in perinatal medicine and neonatal intensive care have markedly improved the survival of extremely preterm infants, yet this progress has simultaneously increased the complexity of managing hematologic and hemostatic disorders in this fragile population. Among the most critical

aspects of care is transfusion medicine, as preterm infants are uniquely predisposed to anemia, thrombocytopenia, and coagulopathy due to physiologic immaturity, rapid growth demands, and the cumulative burden of diagnostic blood sampling [1].Blood transfusions—particularly red blood cell (RBC), platelet, and fresh frozen plasma (FFP) transfusions—are among the most common interventions in the neonatal intensive care unit (NICU). Extremely low birth weight (ELBW) infants may receive multiple transfusions during their hospitalization, often within the first weeks of life. Although transfusions can be life-saving by restoring oxygen-carrying capacity, supporting hemostasis, or correcting coagulopathy, they also carry risks that are accentuated in preterm infants. These include transfusion-associated necrotizing enterocolitis (TANEC), transfusion-related acute lung injury (TRALI), transfusion-associated circulatory overload (TACO), alloimmunization, metabolic instability, and potential long-term neurodevelopmental consequences. The delicate physiological balance of preterm infants necessitates a cautious and evidence-informed approach to transfusion decision-making [2].

Despite decades of clinical research, transfusion thresholds and indications for preterm infants remain variable and often controversial. Landmark trials such as PINT, TOP, and PlaNeT2 have provided important insights, consistently demonstrating that more restrictive transfusion strategies for both RBCs and platelets are generally safe and may reduce harm. Nevertheless, questions persist regarding specific subpopulations—such as critically ill infants, those with severe cardiorespiratory disease, or those undergoing surgery—where transfusion needs may differ. In addition, the pathogenesis of anemia of prematurity, ongoing challenges with iatrogenic blood loss, and the limited reliability of conventional laboratory markers in neonates complicate decisions surrounding transfusion timing and necessity [3].The landscape of neonatal transfusion medicine is further evolving with the emergence of innovative technologies and precision approaches. These include neonatal-specific blood products, pathogen-reduced components, point-of-care hemoglobin and coagulation monitoring, and the development of biomarker-guided algorithms capable of assessing tissue oxygenation and perfusion in real time. Concurrently, strategies aimed at preventing transfusion dependence—such as delayed cord clamping, iron optimization, and judicious phlebotomy reduction—are transforming early neonatal care practices [4].

Aim

To provide a comprehensive overview of transfusion medicine in preterm infants, examining current evidence on indications, risks, and strategies for red blood cell, platelet, and plasma transfusions, and to highlight emerging innovations and future directions aimed at optimizing safety, individualizing care, and improving hematologic and neurodevelopmental outcomes.

Methods

This narrative review was conducted to synthesize current evidence on transfusion medicine in preterm infants, focusing on red blood cell, platelet, and plasma transfusions, associated risks, strategies to minimize exposure, and emerging innovations. A comprehensive literature search was performed using PubMed, Embase, Scopus, and Web of Science databases from inception through November 2025. Search terms included combinations of “preterm infants,” “neonatal transfusion,” “anemia of prematurity,” “platelet transfusion,” “plasma transfusion,” “coagulopathy,” “transfusion risks,” and “emerging technologies in neonatology.”

Eligibility criteria included original research studies, randomized controlled trials, systematic reviews, meta-analyses, clinical guidelines, and relevant expert opinions published in English. Case reports and studies with insufficient data on preterm populations were excluded. Key landmark trials (e.g., PINT, TOP, PlaNeT2) and recent evidence-based guidelines were prioritized to provide an updated synthesis.The literature was reviewed and synthesized narratively, focusing on

physiological mechanisms, clinical indications, transfusion thresholds, adverse effects, preventive strategies, and technological innovations. Emphasis was placed on translating evidence into practical insights for clinical care and identifying gaps for future research.

Anemia of Prematurity and RBC Transfusion

Anemia of prematurity (AOP) represents one of the most frequent hematologic challenges encountered in neonatal care, particularly among extremely low birth weight (ELBW) infants. It arises from a constellation of developmental, physiological, and iatrogenic factors that converge during the first weeks of life. Unlike term infants, who experience a gradual decline in hemoglobin driven by the physiological "anemia of infancy," preterm infants demonstrate a more rapid and profound drop in hematocrit due to the immaturity of their hematopoietic system and the unique stresses of critical illness [5].Several mechanisms underpin the development of AOP. First, erythropoietin (EPO) production—normally stimulated by renal hypoxia-sensing pathways—is markedly blunted in preterm infants. This results in insufficient marrow stimulation and reduced reticulocyte response at a time of accelerated growth and increasing oxygen demand. Second, the fetal red blood cells predominant in preterm infants possess a significantly shorter lifespan compared with adult erythrocytes, leading to faster turnover. Third, iron stores, which are largely accumulated during the third trimester, are inadequate in very preterm neonates, limiting effective erythropoiesis even when EPO levels rise. Finally, iatrogenic phlebotomy losses remain a major contributor: in some ELBW infants, the cumulative volume of blood drawn for laboratory testing may equal or exceed their total circulating blood volume within the first weeks of life [6-7].

Clinically, anemia in preterm infants manifest in diverse ways. Signs may include increasing oxygen and ventilatory requirements, tachycardia, recurrent apnea and bradycardia, poor feeding, delayed weight gain, lethargy, or decreased perfusion. These manifestations often reflect impaired oxygen delivery to tissues and the limited compensatory cardiovascular capacity of the immature neonate [8].Red blood cell (RBC) transfusion remains the cornerstone of treatment for moderate to severe AOP. However, determining the optimal timing and threshold for transfusion has long been debated. Historically, transfusion practices varied widely, with many centers adopting liberal transfusion strategies in attempts to stabilize respiratory function, decrease apnea, or improve weight gain. Over time, concerns about transfusion-associated complications prompted a shift toward more restrictive approaches [9].

Evidence from major clinical trials has substantially informed contemporary practice. The landmark Premature Infants in Need of Transfusion (PINT) trial first demonstrated that restrictive transfusion thresholds could significantly reduce transfusion exposure without worsening short-term outcomes such as death, severe retinopathy of prematurity, or intraventricular hemorrhage. More recently, the Transfusion of Prematures (TOP) trial provided additional clarity by showing no difference in death or neurodevelopmental impairment at 22–26 months of age between infants randomized to high or low hemoglobin thresholds. Together, these findings support the safety of restrictive transfusion strategies for stable, growing preterm infants while challenging assumptions about the clinical benefits of higher transfusion targets [10]. Despite these insights, transfusion decisions remain nuanced. Hemoglobin values alone are insufficient to guide practice, and clinicians must integrate both laboratory data and the infant's clinical condition. For unstable infants—those requiring high ventilatory support, those undergoing surgery, or those demonstrating clear signs of impaired oxygen delivery—a slightly higher transfusion threshold may be appropriate. The heterogeneity of neonatal illness, coupled with the dynamic physiology of preterm infants, underscores the need for individualized assessment rather than rigid adherence to numeric thresholds [11].RBC transfusions themselves are not without risk. Concerns include transfusion-associated necrotizing enterocolitis (TANEC), hemodynamic instability, electrolyte disturbances,

exposure to donor antigens, and potential long-term impacts on neurodevelopment. These risks highlight the importance of careful consideration before transfusion and the parallel need for strategies that reduce transfusion dependence. Approaches such as delayed cord clamping, optimal iron supplementation, early use of erythropoiesis-stimulating agents in selected settings, and minimizing iatrogenic blood loss through micro-sampling have shown promise in mitigating the severity of AOP [12].

Platelet Transfusion in Preterm Infants

Thrombocytopenia is a common hematologic complication in preterm neonates, affecting up to one-third of infants admitted to neonatal intensive care units (NICUs). The condition arises from a combination of decreased platelet production, increased consumption, and, in some cases, immune-mediated destruction. Etiologies include sepsis, necrotizing enterocolitis (NEC), disseminated intravascular coagulation, intrauterine growth restriction, and congenital bone marrow disorders. The clinical consequences of thrombocytopenia can be profound, with an increased risk of bleeding, including intraventricular hemorrhage, gastrointestinal hemorrhage, and mucocutaneous bleeding, particularly in the most immature infants [13].Platelet transfusion has historically been employed liberally in preterm infants with thrombocytopenia, with thresholds ranging from 50,000 to 100,000/μL in many centers. The rationale was to prevent hemorrhagic complications in a population with fragile vasculature and limited hemostatic reserve. However, growing evidence has challenged this paradigm, emphasizing that higher transfusion thresholds may not confer additional protection and may even be associated with harm [14-15].

The landmark PlaNeT2 trial provided pivotal insights into platelet transfusion in preterm neonates. In this multicenter randomized study, infants with severe thrombocytopenia (<50,000/μL) were assigned to receive platelet transfusions at either a higher threshold of 50,000/μL or a lower threshold of 25,000/μL. Surprisingly, the study found that the higher threshold group experienced a significantly higher rate of death or major bleeding events compared with the lower threshold group. This unexpected finding underscored that platelet transfusions, particularly when administered prophylactically in the absence of active bleeding, can trigger inflammatory responses, fluid overload, and possibly adverse microvascular effects [16].Current evidence supports the adoption of **restrictive platelet transfusion strategies** in stable preterm infants, reserving transfusions for those with active bleeding, rapidly falling platelet counts, or critical illness. Clinical decision-making should integrate gestational age, comorbidities, and bleeding risk rather than rely solely on absolute platelet counts. Additionally, consideration of platelet function, rather than number alone, may refine transfusion practices in the future, as emerging research suggests that platelet dysfunction, rather than thrombocytopenia per se, may better predict bleeding risk [17].

While restrictive strategies reduce unnecessary transfusions, they require vigilant monitoring and individualized assessment. Platelet transfusions are not benign; they carry risks of volume overload, alloimmunization, transfusion-related infections, and potential exacerbation of inflammatory pathways. In the context of extremely preterm infants, these adverse effects can contribute to morbidity, highlighting the importance of balancing benefit and risk [18].Emerging approaches to minimize platelet transfusions include reducing iatrogenic blood loss, optimizing nutritional and hematologic support, and exploring adjunctive therapies such as thrombopoietin analogs in clinical trials. Technological advances in bedside platelet function testing and near-patient coagulation monitoring may also guide more precise transfusion decisions, aligning therapy with physiologic need rather than arbitrary thresholds (Table 1).

Table 1: Platelet Transfusion in Preterm Infants

Aspect	Details / Evidence
Indications	Severe thrombocytopenia (<25,000–30,000/µL), active bleeding, rapid platelet count decline, preparation for invasive procedures, sepsis-associated coagulopathy.
Common Thresholds	<25,000/µL in stable preterm infants (restrictive); <50,000/µL in unstable or bleeding infants (liberal). Evidence: PlaNeT2 trial supports restrictive strategy in stable infants.
Transfusion Volume	Typically 10–15 mL/kg of platelets over 30–60 minutes; adjustments for very low birth weight infants to prevent volume overload.
Risks	Volume overload, transfusion-associated infections, alloimmunization, inflammatory reactions, potential increased mortality if liberal transfusion applied unnecessarily.
Evidence-Based Recommendations	Restrictive transfusion strategy is safe in stable preterm infants; transfuse only for clinically significant thrombocytopenia or bleeding. Functional platelet assessment may guide therapy.
Emerging Approaches	Small-volume aliquots, pathogen-reduced platelets, bedside platelet function testing, individualized transfusion guided by physiologic and laboratory parameters.

Plasma and Coagulation Support

Coagulopathy is a frequent concern in preterm infants, particularly among those with extreme prematurity, sepsis, necrotizing enterocolitis, or underlying liver dysfunction. Immature hepatic synthesis, low levels of vitamin K–dependent clotting factors, and the developmental deficiency of natural anticoagulants contribute to a fragile hemostatic balance. Clinically, coagulopathy may manifest as easy bruising, oozing from catheter sites, mucosal bleeding, or, in severe cases, intracranial hemorrhage [18-19].Fresh frozen plasma (FFP) and, less commonly, cryoprecipitate have been the primary therapeutic tools to correct coagulation deficits. Historically, plasma transfusions were administered prophylactically to preterm infants with abnormal coagulation profiles, even in the absence of active bleeding, with the goal of preventing hemorrhagic complications. However, emerging evidence suggests that routine prophylactic plasma transfusions provide little benefit and may expose neonates to unnecessary risks [20].

Current guidelines recommend that FFP transfusion in preterm infants be reserved for **clinically significant bleeding** or prior to invasive procedures in the presence of confirmed coagulopathy. Laboratory indices, including prolonged prothrombin time (PT), activated partial thromboplastin time (aPTT), low fibrinogen levels, and platelet dysfunction, should guide therapy in conjunction with clinical assessment rather than serving as sole triggers. Cryoprecipitate is indicated primarily for infants with severe hypofibrinogenemia or congenital fibrinogen deficiencies, conditions that are rare in the preterm population [21].

Plasma transfusions carry potential risks that warrant careful consideration. These include volume overload, which can precipitate pulmonary edema in infants with limited cardiac reserve; transfusion-related acute lung injury (TRALI); immunologic sensitization; electrolyte disturbances, particularly hypocalcemia and hyperkalemia; and exposure to infectious agents despite modern screening protocols. Furthermore, plasma contains inflammatory mediators that may exacerbate systemic inflammation in vulnerable neonates, potentially contributing to complications such as necrotizing enterocolitis or intraventricular hemorrhage [22].Emerging

strategies aim to reduce the need for plasma transfusions through targeted interventions. These include meticulous fluid management, minimizing iatrogenic blood loss, optimizing nutritional support, and the use of point-of-care coagulation assays such as thromboelastography (TEG) or rotational thromboelastometry (ROTEM). These technologies allow for real-time assessment of the neonate's hemostatic function, enabling clinicians to administer plasma more judiciously and tailor therapy to physiologic need rather than relying solely on standard laboratory thresholds (Table 2) [22].

Table 2: Plasma and Coagulation Support

Aspect	Details / Evidence
Indications	Clinically significant bleeding with coagulopathy, preparation for invasive procedures in presence of abnormal coagulation, congenital clotting factor deficiencies, severe hypofibrinogenemia.
Laboratory Guidance	Prolonged PT/aPTT, low fibrinogen, evidence of functional coagulation deficit; coagulation tests should be interpreted alongside clinical context rather than used alone.
Transfusion Product & Dose	Fresh frozen plasma (FFP): 10–20 mL/kg; Cryoprecipitate: 1–2 units/kg for fibrinogen replacement; dose adjustments based on lab values and infant size.
Risks	Volume overload, transfusion-related acute lung injury (TRALI), electrolyte disturbances (hypocalcemia, hyperkalemia), immunologic reactions, infection risk, potential inflammatory effects.
Evidence-Based Recommendations	Routine prophylactic plasma transfusion is not recommended; transfuse only for active bleeding or confirmed coagulation deficits. Functional hemostatic monitoring (TEG/ROTEM) improves precision.
Emerging Strategies	Point-of-care coagulation assays, targeted plasma therapy, minimized transfusion volumes, integration with predictive algorithms, and individualized risk assessment to reduce exposure.

Risks Associated with Transfusion in Preterm Infants

While transfusions are often lifesaving in preterm infants, they are not without risk. The immature physiology of preterm neonates amplifies vulnerability to both immediate and long-term complications associated with red blood cell (RBC), platelet, and plasma transfusions. Awareness of these risks is critical to inform judicious transfusion practices and to guide strategies for minimizing exposure (Table 3).

Table 3: Risks Associated with Transfusion in Preterm Infants:

Risk Category	Details / Evidence
Transfusion-Associated Necrotizing Enterocolitis (TANEC)	Occurs within 24–48 hours of RBC transfusion in some preterm infants; mechanisms include mesenteric hypoperfusion, reperfusion injury, oxidative stress, and inflammation. Feeding management during transfusion may reduce risk.
Pulmonary Complications	Transfusion-related acute lung injury (TRALI) – rare but serious; Transfusion-associated circulatory overload (TACO) – more common in ELBW infants due to limited cardiac/pulmonary reserve.
Infectious Risks	Despite rigorous screening, residual risk of bacterial contamination (especially platelets) and viral transmission exists. Use of CMV-negative, leukoreduced, and pathogen-reduced products reduces risk.
Immunologic Reactions	Alloimmunization, hemolytic reactions, and allergic responses; may complicate future transfusions or maternal-fetal compatibility.
Metabolic and Biochemical Complications	Electrolyte disturbances (hypocalcemia, hyperkalemia), acid-base imbalance, citrate toxicity; preterm infants are particularly sensitive due to immature renal and metabolic function.
Inflammatory and Hemodynamic Effects	Exposure to stored blood products may trigger systemic inflammation, endothelial activation, and microvascular dysfunction. Hemodynamic instability (hypotension, tachycardia) can occur.
Neurodevelopmental Concerns	Multiple transfusions in extremely low birth weight infants may influence cerebral oxygenation and white matter development; evidence from TOP and PINT trials shows no major impairment with restrictive strategies, but long-term subtle effects remain under study.

Transfusion-Associated Necrotizing Enterocolitis (TANEC)

One of the most extensively studied complications is transfusion-associated necrotizing enterocolitis. Observational studies and meta-analyses have suggested that a subset of preterm infants may develop NEC within 24–48 hours of an RBC transfusion, particularly when enteral feeds are not carefully managed. Proposed mechanisms include mesenteric hypoperfusion, reperfusion injury, oxidative stress, and inflammatory cytokine activation. Although causality remains debated, many NICUs have adopted the practice of temporarily withholding feeds during transfusion in high-risk infants to mitigate this potential complication [23].

Pulmonary Complications

Transfusion-related acute lung injury (TRALI), although rare in neonates, represents a potentially life-threatening reaction characterized by acute pulmonary edema and hypoxemia. Volume overload leading to transfusion-associated circulatory overload (TACO) is a more common concern in preterm infants, who possess limited cardiac and pulmonary reserve. Even modest fluid shifts during transfusion can precipitate respiratory distress, worsening oxygenation, or the need for mechanical ventilation [24].

Infectious and Immunologic Risks

Despite rigorous donor screening and modern pathogen reduction techniques, transfusions remain a potential source of infectious exposure, including bacterial contamination (particularly in platelet products) and cytomegalovirus

transmission. Leukoreduction, irradiation, and use of CMV-negative blood have mitigated many of these risks, yet vigilance remains essential. Additionally, transfusions may trigger immunologic reactions such as hemolysis, allergic responses, and alloimmunization, which can complicate future transfusions or maternal-fetal compatibility in subsequent pregnancies [25].

Metabolic and Biochemical Complications

Transfusions can induce electrolyte disturbances, particularly hyperkalemia and hypocalcemia, as well as acid-base imbalances due to citrate toxicity. Preterm infants are particularly sensitive to these perturbations due to immature renal function and limited metabolic buffering capacity. Rapid transfusion rates or large-volume transfusions exacerbate these risks [26].

Inflammatory and Hemodynamic Effects

Exposure to allogeneic blood products may provoke systemic inflammatory responses in preterm neonates. Pro-inflammatory mediators, accumulated during storage of blood products, can contribute to endothelial activation, microvascular dysfunction, and organ injury. Hemodynamic instability, including hypotension or tachycardia, can occur during transfusion, especially in infants with limited cardiovascular reserve or concurrent illness [27].

Neurodevelopmental Considerations

Long-term neurodevelopmental outcomes in transfused preterm infants have been a focus of recent research. While major trials, including the TOP study, indicate no significant difference in neurodevelopmental impairment between restrictive and liberal RBC transfusion strategies, concerns persist regarding subtle impacts on cerebral oxygenation, white matter development, and neuroinflammatory pathways. The cumulative effect of multiple transfusions in extremely low birth weight infants may influence these outcomes, emphasizing the need for careful, individualized transfusion practices [28-30].

Balancing Risks and Benefits

The diverse spectrum of transfusion-related complications underscores the necessity of balancing immediate therapeutic benefits against potential harm. Evidence supports adopting restrictive and individualized transfusion thresholds for RBCs, platelets, and plasma, coupled with meticulous monitoring and strategies to minimize unnecessary exposure. Measures such as reducing phlebotomy losses, optimizing nutrition and erythropoiesis, and employing advanced monitoring tools can help mitigate these risks while preserving the benefits of transfusion in this vulnerable population [31].

Strategies to Minimize Transfusion Requirements

Reducing transfusion exposure in preterm infants is a critical component of modern neonatal care, aimed at balancing the therapeutic benefits of transfusions with the risk of adverse outcomes. A multi-faceted approach, combining preventive, supportive, and technological strategies, has emerged to minimize the need for red blood cell, platelet, and plasma transfusions in this highly vulnerable population [32].A major contributor to transfusion requirement is iatrogenic blood loss from frequent laboratory testing. Extremely low birth weight infants may lose a significant proportion of their circulating blood volume in the first weeks of life. Strategies to mitigate this include micro-sampling techniques, the use of point-of-care testing, and consolidating laboratory investigations to limit the number of blood draws. Innovations such as in-line blood sampling systems further reduce cumulative phlebotomy loss, preserving endogenous hematologic reserves [33].

Supporting endogenous erythropoiesis is another cornerstone of transfusion-sparing strategies. Delayed cord clamping and umbilical cord milking at birth enhance neonatal blood volume and iron stores, reducing early anemia. Optimized nutritional support, particularly with iron, folate, and vitamin B12, fosters red blood cell production. In select high-risk infants,

recombinant erythropoietin or darbepoetin may stimulate erythropoiesis, although their routine use remains limited by cost, logistical challenges, and ongoing questions regarding long-term safety and neurodevelopmental impact [34].Adopting restrictive, evidence-based transfusion thresholds has been shown to reduce unnecessary exposure without compromising clinical outcomes. Landmark trials such as PINT, TOP, and PlaNeT2 demonstrate that lower hemoglobin and platelet thresholds are safe for stable preterm infants, emphasizing the importance of integrating laboratory parameters with the infant's clinical status, oxygen requirements, and hemodynamic stability in transfusion decision-making [35].

Judicious use of plasma and coagulation products is also essential. Prophylactic plasma transfusion is generally discouraged in the absence of active bleeding or significant coagulation abnormalities. Functional hemostatic assessment using thromboelastography (TEG) or rotational thromboelastometry (ROTEM) allows targeted therapy, ensuring that plasma or platelet transfusions are administered only when clinically indicated [34].Finally, technological innovations and continuous monitoring are enhancing transfusion stewardship. Near-infrared spectroscopy (NIRS) permits real-time evaluation of tissue oxygenation, potentially identifying infants who can safely tolerate lower hemoglobin levels. Predictive algorithms and integrated monitoring platforms may soon allow proactive planning of transfusions based on individual physiologic need rather than rigid laboratory thresholds [35].

Emerging Innovations and Future Directions

The field of neonatal transfusion medicine is rapidly evolving, driven by the need to optimize care for preterm infants while minimizing the inherent risks of blood product exposure. Traditional transfusion practices, largely guided by static laboratory thresholds, are giving way to individualized, physiologically informed strategies that leverage technological advances, biomarker insights, and precision medicine approaches [36].One major innovation is the development of neonatal-specific blood products. Standard adult blood components are often suboptimal for preterm infants due to storage-related biochemical changes, volume mismatches, and differences in hemoglobin composition. Current efforts focus on producing RBC units with shorter storage duration, improved preservation of fetal hemoglobin, and reduced oxidative stress. Similarly, small-volume platelet and plasma products, as well as pathogen-reduced components, are increasingly used to limit the risk of volume overload, immunologic reactions, and transfusion-transmitted infections [37].

Biomarker-guided transfusion represents another promising frontier. Technologies such as near-infrared spectroscopy (NIRS) allow continuous assessment of cerebral and systemic tissue oxygenation, providing functional measures of anemia and perfusion that go beyond conventional hemoglobin or platelet counts. Complementary approaches using metabolic indicators, microvascular perfusion assessment, and coagulation function tests enable clinicians to tailor transfusions based on physiologic need rather than arbitrary numeric thresholds [38].Advances in bedside monitoring and point-of-care diagnostics further facilitate precision transfusion. Thromboelastography (TEG) and rotational thromboelastometry (ROTEM) provide real-time functional assessment of the coagulation cascade, guiding plasma and platelet therapy more accurately. Micro-sampling and minimally invasive laboratory techniques reduce iatrogenic blood loss, a major driver of anemia and subsequent transfusion. Emerging artificial intelligence algorithms and predictive models are also being explored to anticipate transfusion requirements by integrating continuous physiologic, laboratory, and clinical data [39].

Adjunctive strategies aimed at preventing transfusion dependence complement these technological innovations. Delayed cord clamping and umbilical cord milking enhance neonatal blood volume and iron stores. Optimized nutritional support, including iron, folate, and vitamin B12 supplementation, promotes endogenous erythropoiesis. In selected high-risk

infants, pharmacologic interventions such as recombinant erythropoietin or thrombopoietin analogs may stimulate red blood cell and platelet production, though long-term safety and efficacy remain under investigation [40].

Conclusion

Transfusion medicine remains a cornerstone of care for preterm infants, addressing anemia, thrombocytopenia, and coagulopathy in this highly vulnerable population. Contemporary evidence supports a more restrictive and individualized approach to red blood cell, platelet, and plasma transfusions, emphasizing the balance between immediate clinical benefit and potential short- and long-term risks. Landmark trials demonstrate that lower transfusion thresholds are generally safe, reducing exposure without compromising survival or neurodevelopmental outcomes.

Emerging innovations—including neonatal-specific blood products, biomarker-guided decision-making, advanced bedside monitoring, and predictive analytics—offer promising avenues to further individualize care, minimize transfusion requirements, and optimize physiologic outcomes. Preventive strategies such as delayed cord clamping, minimizing iatrogenic blood loss, and promoting endogenous erythropoiesis complement these advances, collectively aiming to reduce transfusion dependence.

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