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Challenges in red blood cell transfusion in resource-limited settings: A narrative review



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ABSTRACT

Introduction: Red blood cell (RBC) transfusion remains an essential life-saving intervention for patients with hemorrhage, anemia, surgery-related blood loss, and chronic disease. In resource-limited settings, however, transfusion practice is shaped by constraints that affect safety, availability, compatibility testing, and timely delivery. This narrative review aims to examine the major challenges affecting RBC transfusion in resource-limited settings, with particular attention to blood safety, supply sustainability, compatibility testing, infrastructure limitations, logistics, hemovigilance, and sociocultural barriers to donation and transfusion.

Methods: This narrative review synthesizes current challenges in RBC transfusion in resource-limited settings, with emphasis on transfusion safety, blood supply systems, immunohematological compatibility, infrastructure, logistics, and sociocultural barriers to donation.

Results: Key challenges include persistent risks of transfusion-transmitted infections where screening coverage, laboratory quality assurance, and pathogen detection capacity are limited. Low voluntary donation rates, weak donor retention, seasonal fluctuations, and inadequate storage capacity frequently drive blood shortages. Compatibility-related problems, including limited blood grouping, crossmatching, and antibody screening, may increase the risk of acute or delayed transfusion reactions. Infrastructure limitations, such as insufficient cold chain systems, unreliable transportation, limited trained personnel, and fragmented hemovigilance, further compromise timely and safe access to RBC products. Cultural beliefs, misconceptions, and ethical concerns may also reduce donor participation and acceptance of transfusion.

Conclusion: RBC transfusion in resource-limited settings requires more than blood availability; it depends on integrated systems that strengthen donor recruitment, screening quality, compatibility testing, storage, transport, and hemovigilance. Targeted, context-appropriate improvements are essential to make transfusion safer, more reliable, and more equitable.

Keywords: Blood compatibility, blood safety, blood supply, red blood cell transfusion, resource-limited settings.

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INTRODUCTION

Blood transfusion is a cornerstone of modern clinical practice, involving the administration of blood or its components to restore physiological function in patients with acute or chronic conditions. It is commonly indicated in cases of severe anemia, trauma, major surgery, and obstetric complications, contributing significantly to reduced morbidity and mortality worldwide.¹ Red blood cell (RBC) transfusion is an essential component of modern clinical care. It remains a life-saving intervention for patients with acute hemorrhage, severe anemia, major surgery, trauma, obstetric

bleeding, malignancy, and chronic hematologic disorders. Its clinical value is well established, but transfusion is not a risk-free intervention because it requires a coordinated system involving donor recruitment, blood collection, infectious disease screening, component preparation, compatibility testing, storage, transport, clinical decision-making, and post-transfusion monitoring. Recent global data from the World Health Organization reported that approximately 120.4 million blood donations are collected worldwide each year; however, 36% of these donations are collected in high-income countries, which represent only 15% of the global population.² This imbalance highlights

that transfusion safety and availability are not merely clinical issues, but also reflect broader health-system capacity.

The disparity is more evident when blood donation rates are compared across income groups. The median donation rate is reported to be 28.9 donations per 1,000 population in high-income countries, compared with 8.5 in lower-middle-income countries and only 4.5 in low-income countries. These figures indicate that many resource-limited settings face structural shortages of safe blood, particularly during emergencies, obstetric complications, pediatric anemia, and surgical care. Although voluntary unpaid blood donation has increased globally,

59 countries still collect more than 50% of their blood supply from family/ replacement or paid donors, which may affect both supply stability and transfusion safety.² Therefore, the challenge in these settings is not only obtaining sufficient RBC units, but also ensuring that available units are safe, compatible, and delivered in a timely manner.

Advances in transfusion medicine, particularly the adoption of component therapy and improved donor screening, have enhanced both the safety and efficacy of this intervention.³ Existing report has extensively discussed transfusion thresholds, restrictive versus liberal transfusion strategies, and patient blood management, particularly in high-income healthcare systems.⁴ Nevertheless, challenges remain, including variability in transfusion practices, risks of adverse reactions, and limited access to safe blood in resource-constrained settings.⁵ Previous studies emphasize the importance of evidence-based transfusion strategies, such as restrictive transfusion thresholds, to optimize patient outcomes while minimizing unnecessary exposure.⁶ However, these recommendations often assume the presence of reliable laboratory infrastructure, trained personnel, uninterrupted cold chains, standardized compatibility testing, and functioning hemovigilance systems. In resource-limited settings, these assumptions may not consistently apply. Limited screening capacity, reagent shortages, delayed crossmatching, inadequate storage facilities, transportation barriers, and weak adverse-event reporting systems frequently constrain the implementation of evidence-based transfusion practice.^{2,7} As a result, transfusion decisions may be influenced not only by clinical indication, but also by the availability and reliability of the blood system.

The literature gap lies in the limited synthesis of how safety, supply, immunohematological compatibility, infrastructure, and sociocultural factors interact to shape RBC transfusion practice in resource-limited settings. This is important because RBC products are among the most commonly transfused blood components and are frequently needed in urgent, high-risk clinical

situations. The WHO also emphasizes that many patients still lack timely access to safe blood, particularly in lower-income countries, despite global progress in voluntary blood donation and screening systems.^{2,7} Furthermore, the integration of haemovigilance systems and continuous quality improvement initiatives has been shown to improve transfusion safety.⁸ A narrative review approach is therefore appropriate to critically integrate evidence across clinical practice, blood service organization, laboratory capacity, and public health perspectives. This narrative review aims to examine the major challenges affecting RBC transfusion in resource-limited settings, with particular attention to blood safety, supply sustainability, compatibility testing, infrastructure limitations, logistics, hemovigilance, and sociocultural barriers to donation and transfusion.

METHODS

Study Design

This article was conducted as a narrative review to synthesize current knowledge regarding RBC transfusion challenges in resource-limited settings. The review focused on key domains relevant to transfusion practice, including blood safety, blood supply, donor recruitment, transfusion-transmitted infections, immunohematological compatibility, laboratory capacity, storage and transportation systems, hemovigilance, and sociocultural barriers affecting donation and transfusion.

Literature Search

Relevant literature was identified through searches of PubMed/MEDLINE, Scopus, Google Scholar, and official reports from international health organizations, particularly the World Health Organization. Search terms included combinations of “red blood cell transfusion,” “blood transfusion,” “blood safety,” “blood supply,” “compatibility testing,” “transfusion-transmitted infections,” “hemovigilance,” “resource-limited settings,” “low- and middle-income countries,” and “blood donation.” Additional references were identified by reviewing the reference lists of relevant articles and reports.

Study Selection

Articles were considered for inclusion if they discussed RBC transfusion practice, transfusion safety, blood availability, compatibility testing, infrastructure limitations, or transfusion-related health system challenges in resource-limited or low- and middle-income settings. Priority was given to recent publications, global reports, review articles, guidelines, and studies with direct relevance to transfusion services and clinical practice. Articles focusing exclusively on highly specialized transfusion technologies without relevance to resource-limited settings were excluded.

Data Synthesis

The findings were synthesized narratively rather than statistically because of the heterogeneity of study designs, settings, outcomes, and reported challenges. The selected literature was organized into major thematic areas, including safety and infectious risk, blood supply and donor systems, compatibility and immunohematological challenges, infrastructure and logistics, hemovigilance, and sociocultural considerations. This approach allowed integration of evidence from clinical, laboratory, public health, and health system perspectives to provide a comprehensive overview of RBC transfusion challenges in resource-limited settings.

RESULTS AND DISCUSSION

History

The history of blood transfusion reflects centuries of scientific experimentation, discovery, and clinical advancement. Early attempts in the 17th century involved transfusing animal blood into humans, often resulting in severe or fatal reactions due to the absence of knowledge about blood compatibility.⁹ A breakthrough occurred in the early 19th century when James Blundell successfully performed human-to-human transfusions to treat postpartum hemorrhage.¹⁰ However, the practice remained risky until the discovery of the ABO blood group system by Karl Landsteiner in 1901, which marked a turning point in transfusion safety.¹¹ Further progress followed with

the identification of the Rh factor and the use of anticoagulants during World War I, enabling blood preservation and wider clinical application.¹² The establishment of blood banks and improved screening methods in the 20th century significantly enhanced both safety and accessibility.¹³ These milestones have collectively transformed blood transfusion into a reliable and essential component of modern medicine.

The development of red blood cell transfusion is most relevant to modern practice when viewed through milestones that improved safety, compatibility, preservation, and system organization. Early transfusion attempts were limited by the absence of blood group knowledge, but the discovery of the ABO blood group system by Landsteiner in 1901 fundamentally changed transfusion from an experimental procedure into a compatibility-based intervention. The later identification of the Rh system, introduction of anticoagulant-preservative solutions, and establishment of blood banks enabled blood storage, inventory management, and wider clinical use. These advances remain central to current transfusion systems because modern safety still depends on accurate blood grouping, crossmatching, screening, cold-chain preservation, and standardized clinical governance. In resource-limited settings, the historical progress of transfusion medicine is unevenly implemented. At the same time, compatibility testing and blood banking are standard in principle; shortages of reagents, trained staff, storage equipment, and quality assurance systems may limit their practical application.¹⁰ Thus, the history of transfusion is not only a record of scientific progress, but also a reminder that transfusion safety depends on health-system capacity, not merely on scientific discovery.

Indications for Red Cell Transfusion

Red cell transfusion is primarily indicated to improve oxygen delivery in patients with reduced red blood cell mass or impaired oxygen-carrying capacity. Common indications include severe anemia resulting from acute blood loss, chronic diseases, or nutritional deficiencies.¹⁴ It is also essential in the management of patients

undergoing major surgery or experiencing trauma with significant hemorrhage.¹⁵ In critically ill patients, transfusion decisions are often guided by hemoglobin thresholds and clinical symptoms such as fatigue, dyspnea, and hemodynamic instability.¹⁶ Additionally, individuals with hematological disorders, including sickle cell disease and thalassemia, may require transfusions for disease management and prevention of complications.¹⁷ Evidence-based guidelines recommend restrictive transfusion strategies to optimize outcomes and minimize risks associated with unnecessary transfusions.¹⁸

Current red cell transfusion practice should be guided by clinical context, hemoglobin concentration, active bleeding status, comorbid disease, and evidence-based transfusion thresholds rather than by anemia alone. The 2023 AABB international guidelines recommend a restrictive transfusion strategy for most hemodynamically stable hospitalized adults, with transfusion considered when hemoglobin is below 7 g/dL; thresholds of 7.5 g/dL may be used in cardiac surgery and 8 g/dL in orthopedic surgery or pre-existing cardiovascular disease. These recommendations were based on 45 randomized controlled trials involving 20,599 adults, in which restrictive thresholds of 7–8 g/dL generally did not worsen patient-important outcomes compared with liberal thresholds of 9–10 g/dL.³ In resource-limited settings, restrictive transfusion practice has additional relevance because unnecessary transfusion can deplete already limited blood supplies and expose patients to avoidable risks. However, thresholds should not replace clinical judgment, particularly in active hemorrhage, hemodynamic instability, severe hypoxemia, acute coronary syndromes, obstetric bleeding, and chronic transfusion-dependent disorders. Therefore, the indication for red cell transfusion should be framed as a balance between physiological need, expected benefit, transfusion risk, and local blood availability.

Red Cell Antigens and Antibodies

Red cell antigens are specific molecules located on the surface of red blood cells that play a crucial role in blood group classification and transfusion

compatibility. These antigens, primarily composed of proteins and carbohydrates, are inherited genetically and vary among individuals.¹⁹ The most clinically significant systems include the ABO and Rh blood group systems, which are essential in determining donor–recipient compatibility and preventing adverse transfusion reactions.²⁰ Other blood group systems, such as Kell, Duffy, and Kidd, may also contribute to immune responses, particularly in patients receiving repeated transfusions.²¹ The presence or absence of these antigens can stimulate antibody production, leading to hemolytic transfusion reactions if incompatible blood is administered.²² Therefore, accurate identification of red cell antigens is critical for safe transfusion practice.²³

Red cell antibodies are immunoglobulins produced by the immune system in response to foreign red blood cell antigens, often following transfusion, pregnancy, or transplantation.²⁴ They are broadly classified into naturally occurring antibodies, such as those in the ABO system, and immune antibodies formed after exposure to incompatible antigens.²⁵ Clinically significant antibodies are typically of the IgG type. They can cross the placenta or react at body temperature, leading to hemolytic transfusion reactions or hemolytic disease of the fetus and newborn.²⁶ Antibodies directed against antigens in systems such as Rh, Kell, Kidd, and Duffy are particularly important in transfusion medicine.²⁷ The detection and identification of these antibodies through screening and crossmatching procedures are essential to ensure compatibility and prevent adverse reactions.²⁸ In patients requiring repeated transfusions, alloimmunization remains a major concern, complicating the selection of compatible blood²⁶. Therefore, careful antibody screening and adherence to transfusion protocols are critical for patient safety.

Red cell antigens and antibodies are clinically important because they directly determine transfusion compatibility and influence the risk of hemolytic reactions, delayed transfusion reactions, and difficulty finding compatible blood. While ABO and RhD matching prevents the most immediate and severe incompatibility

reactions, other antigen systems, such as Rh variants, Kell, Kidd, Duffy, and MNS become especially important in patients requiring repeated transfusions. Alloimmunization is a major challenge in transfusion-dependent populations, including patients with thalassemia and sickle cell disease, because newly formed antibodies complicate crossmatching and may delay access to compatible blood. A systematic review in transfusion-dependent thalassemia reported an overall red cell alloimmunization prevalence of 11.4%, with Rh and Kell antibodies accounting for most cases.²⁹ More recent evidence also emphasizes alloimmunization as a persistent transfusion challenge in chronically transfused patients, particularly where extended antigen typing and antibody identification are not routinely available.³⁰ In resource-limited settings, the clinical impact is amplified because laboratories may rely mainly on ABO/RhD typing and immediate-spin or basic crossmatching. At the same time, extended phenotype matching, antibody panels, and rare donor registries may be unavailable or unaffordable. Consequently, immunohematology should be discussed not only as a laboratory concept, but as a practical determinant of transfusion access and safety.

Challenges of RBC Transfusion

Red cell transfusion is a life-saving intervention, but it is associated with several significant challenges that affect its safety and accessibility. One major issue is compatibility, as mismatched transfusions can lead to severe hemolytic reactions due to antigen-antibody interactions.²² Despite rigorous testing, alloimmunization in patients receiving repeated transfusions complicates the identification of compatible blood.³¹ Additionally, there remains a risk of transfusion-transmitted infections, including viral and bacterial pathogens, particularly in settings with limited screening capacity.³² Shortages of donors and inadequate blood supply further hinder timely transfusion, especially in low- and middle-income countries.⁵ Storage challenges, such as maintaining optimal temperature and preventing degradation of red cells, also

impact blood quality and availability.³³ Furthermore, limited skilled personnel and inadequate training in transfusion practices can compromise patient safety in resource-constrained settings.³⁴ Financial constraints, including insufficient funding and lack of comprehensive insurance coverage, restrict access to safe transfusion services.³⁵ Addressing these challenges requires improved infrastructure, enhanced training, robust screening systems, and increased investment in healthcare systems.

The challenges of red cell transfusion in resource-limited settings can be grouped into four main categories, i.e. safety, supply, infrastructure, and workforce or governance. Safety challenges include transfusion-transmitted infections, incomplete screening coverage, limited external quality assessment, and weak hemovigilance. WHO recommends mandatory screening for HIV, hepatitis B, hepatitis C, and syphilis, yet recent global data show that 10 reporting countries are still unable to screen all donated blood for one or more of these infections. Only 63% of blood screening laboratories globally participate in external quality assessment schemes, with participation varying substantially by country income level.⁷ These gaps indicate that infection risk is not only related to pathogen prevalence, but also to the reliability of testing systems, reagent supply, laboratory quality control, and regulatory oversight.

Supply challenges remain equally important. WHO reported that approximately 120.4 million blood donations are collected globally, but 36% are collected in high-income countries, which represent only 15% of the global population. Donation rates also differ markedly, from 28.9 donations per 1,000 population in high-income countries to only 4.5 per 1,000 in low-income countries. In addition, 59 countries still collect more than 50% of their blood supply from family/replacement or paid donors, which may reduce supply stability and safety compared with regular voluntary unpaid donation.⁷ Limited donor recruitment systems, low public awareness, cultural misconceptions, weak donor retention, and inadequate funding for national blood services drive these shortages.

Infrastructure barriers include inadequate cold-chain systems, limited component separation capacity, unreliable transportation, poor inventory systems, and insufficient blood bank coverage outside urban centers. WHO data show that only 52% of blood collected in low-income countries is separated into components, compared with 98% in high-income countries. This limits the efficient use of donated blood and may increase wastage or inappropriate product use. Workforce and governance limitations further compound these problems. Only 40% of hospitals performing transfusions globally have transfusion committees, and only 52% of reporting countries have a hemovigilance system.⁷ In low-resource environments, the absence of structured monitoring makes it difficult to identify near-miss events, transfusion reactions, inappropriate transfusions, and system failures. Therefore, the central problem is not a single technical weakness, but a chain of interdependent vulnerabilities across donor recruitment, testing, storage, clinical use, and post-transfusion surveillance. **Table 1** shows a summary of RBC transfusion challenges in limited-resource settings.

Future-Perspectives/ Recommendations

Future strategies to address the challenges of red cell transfusion focus on innovation, improved safety, and sustainability of blood supply systems. One promising approach is the development of blood substitutes, such as hemoglobin-based oxygen carriers, which can temporarily replace the oxygen-carrying function of red cells in emergencies.³⁶ Additionally, enzyme-modified red blood cells offer potential for universal transfusion by converting blood group antigens, particularly from group A or B to group O, thereby reducing compatibility issues.³⁷ Advances in pathogen reduction technologies also aim to minimize the risk of transfusion-transmitted infections.³⁸ Furthermore, improved donor recruitment strategies, including voluntary non-remunerated donation campaigns, can help alleviate blood shortages.³⁹ Strengthening storage technologies and cold chain systems will enhance the shelf life and quality of blood

products. Investment in training healthcare personnel and expanding transfusion services in low-resource settings is equally critical.⁴⁰ Collectively, these innovations and systemic improvements hold promise for safer and more accessible transfusion practices globally.

Future strategies should prioritize feasible system strengthening rather than relying primarily on advanced technologies that may be difficult to implement in low-resource settings. Blood substitutes, enzyme-modified universal red cells, and advanced pathogen-reduction technologies are scientifically promising. Still, their current applicability in resource-limited settings is constrained by cost, regulatory requirements, manufacturing complexity, and infrastructure needs. For many low- and middle-income countries, the more immediate priority is to strengthen national blood policies, improve voluntary non-remunerated donor recruitment, ensure consistent screening for transfusion-transmitted infections, expand compatibility testing, maintain cold-chain reliability, and establish practical hemovigilance systems. WHO similarly recommends coordinated national blood systems, quality-assured screening, voluntary unpaid donation, rational clinical use of blood, and stepwise implementation of quality systems.⁷

Practical recommendations should therefore be directly linked to the challenges identified. To address shortages, countries should invest in repeat voluntary donor programs, community education, mobile blood collection, and donor retention systems. To improve safety, blood services should prioritize reliable test kits, external quality assessment, standard operating procedures, and mandatory screening for HIV, HBV, HCV, and syphilis. To reduce compatibility-related complications, extended Rh and Kell matching may be prioritized for chronically transfused patients when full molecular typing is not feasible. To improve clinical use, hospitals should implement restrictive transfusion policies, transfusion committees, audit systems, and patient blood management adapted to local resources. In this way, innovation should be understood not only as new technology, but also as better organization, governance, training, and

Table 1. The summary of RBC transfusion challenges in limited-resource settings

Challenge domain	Key problem	Underlying cause in resource-limited settings	Proposed solution
Blood safety	Transfusion-transmitted infections	Incomplete screening, reagent shortages, limited quality assurance	Mandatory screening, external quality assessment, standardized SOPs
Blood supply	Shortage of RBC units	Low voluntary donation, dependence on replacement donors, weak donor retention	Repeat voluntary donor programs, public education, mobile donation systems.
Compatibility	Alloimmunization and delayed compatible blood	Limited antibody screening, lack of extended phenotype matching	Prioritize Rh/Kell matching for chronically transfused patients
Infrastructure	Poor storage and delayed distribution	Weak cold chain, limited component processing, transport barriers	Inventory systems, cold-chain investment, regional blood networks
Workforce and governance	Unsafe or inconsistent transfusion practice	Limited training, weak hemovigilance, lack of transfusion committees	Staff training, hospital transfusion committees, adverse-event reporting

RBC: red blood cell, SOP: standard operational procedure

accountability across the transfusion chain.

Strengths and Limitations of this Review

The strength of this narrative review is its integrated discussion of red cell transfusion challenges across clinical, laboratory, public health, and health-system domains. By focusing on resource-limited settings, this review highlights practical barriers that are often underemphasized in guideline-centered discussions developed in high-resource contexts. However, this review also has limitations. As a narrative review, it does not apply systematic search, study selection, or meta-analysis methods, and therefore may be subject to selection bias. The heterogeneity of available evidence across countries, blood service models, and healthcare systems also limits direct generalization. Nevertheless, the review provides a structured synthesis that may guide future research, policy development, and context-specific transfusion improvement strategies.

CONCLUSION

Red blood cell transfusion in resource-limited settings is shaped by interconnected challenges across the transfusion chain, including donor recruitment, blood supply, infectious screening, compatibility testing, storage, transportation, clinical decision-making, and hemovigilance. This review highlights that safe transfusion depends not only on the availability of blood units, but also on reliable laboratory systems, trained personnel, rational transfusion practice, and effective governance. Clinically, restrictive transfusion strategies and context-based decision-making may reduce unnecessary transfusions and preserve limited blood supplies. From a policy perspective, strengthening voluntary donor programs, national blood regulation, quality assurance, cold-chain systems, and adverse-event reporting should be prioritized over costly technologies that may not be feasible in low-resource contexts. Future research should focus on locally adaptable interventions, including donor retention models, simplified compatibility strategies

for chronically transfused patients, and practical hemovigilance systems. Overall, improving red blood cell transfusion in resource-limited settings requires a system-strengthening approach that links safety, sufficiency, compatibility, and equitable access.

DISCLOSURES

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The authors declare there was no external funding in this study.

CONFLICTS OF INTEREST

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

AUTHORS CONTRIBUTIONS

AOOL and AOO were involved in concept design and supervision of the manuscript. SAU and DCO drafted the original manuscript. All authors performed data curation and agreed for this final version of the manuscript to be submitted to this journal.

ETHICAL CONSIDERATION

Not applicable.

GENERATIVE AI USAGE

We declare that there is no AI use in this study.

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