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The near-infrared spectroscopy to evaluate neonatal improvement after transfusion: a systematic review and meta-analysis

Shao Cong Zheng[1] and Shan He[2*]

Abstract

Background Anemia of prematurity (AOP) is a common issue in neonatal intensive care units (NICUs) globally, associated with significant morbidity and mortality. Near-infrared spectroscopy (NIRS) has emerged as a noninvasive, real-time monitoring tool to assess tissue oxygenation and blood flow, potentially providing valuable insights into the impact of red blood cell transfusions in preterm infants with anemia. This study aimed to evaluate the effectiveness of NIRS in assessing improvements in preterm infants after red blood cell transfusions.

Methods This study followed a systematic review and meta-analysis design, adhering to the Cochrane Handbook for Systematic Reviews of Interventions and PRISMA guidelines. No geographic or temporal restrictions were imposed during the search. The final included studies spanned 2008–2017 and originated from four countries. A total of 214 articles were initially identified, and nine prospective observational studies were included in the final analysis. These studies focused on preterm infants diagnosed with anemia who required red blood cell transfusion therapy. The sample sizes in these studies ranged from 10 to 35 infants. The primary outcome was the changes in NIRS readings before and after transfusion. The secondary outcomes included changes in heart rate (HR), saturation of pulse oxygen (SPO_2), and hemoglobin (Hb) pre- and post-transfusion.

Results Meta-analysis demonstrated significant post-transfusion increases in $CrSO_2$ (mean difference [MD] = -8.51, 95% CI: -12.34 to -4.68) and $SrSO_2$ (MD = -15.68, 95% CI: -20.12 to -11.24). Subgroup analyses revealed greater improvements in $CrSO_2$ for infants with higher baseline anemia severity (MD = -14.76, 95% CI: -18.19 to -11.33) and in $SrSO_2$ (MD = -22.79, 95% CI: -26.96 to -18.62). Cerebral fractional tissue oxygen extraction (cFTOE) and splanchnic fractional tissue oxygen extraction (sFTOE) also showed significant changes. Hemoglobin levels increased post-transfusion (MD = -2.89, 95% CI: -3.21 to -2.57), while heart rate and peripheral oxygen saturation (SPO_2) remained unchanged.

Conclusions The findings suggest that NIRS is a reliable tool for assessing the impact of red blood cell transfusions in preterm infants.

Trial Registration PROSPERO (ID: CRD42024596069).

Keywords Near-Infrared Spectroscopy, Preterm Infants, Transfusion, Meta-Analysis, Tissue Oxygenation, Anemia

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Introduction

Anemia of prematurity (AOP) is a common issue in neonatal intensive care units (NICUs) globally [1] and is associated with significant morbidity and mortality in preterm infants in preterm infants [2]. Tissue hypoxia caused by anemia can negatively impact the development and function of multiple organs [3]. In the brain, hypoxia may result in neuronal damage, impede neural development, and increase the risk of neurological sequelae, including cognitive impairment and delayed motor development in the long term [4, 5]. Additionally, the gastrointestinal system is particularly vulnerable to the effects of hypoxia caused by anemia. Several studies have demonstrated that anemia can elevate the incidence of necrotizing enterocolitis(NEC) in neonates [6].

Red cell blood transfusion is crucial for managing various conditions in newborns, including anemia [7], hemolytic disease, and other blood-related disorders [8]. The effectiveness of transfusion is commonly assessed through improvements in clinical signs and physiological parameters [9]. However, evaluating the impact of transfusion on neonatal health remains challenging, owing to the vulnerabilities of the neonatal population and the limitations of traditional monitoring techniques [10, 11].

Near-infrared spectroscopy (NIRS) has emerged as a noninvasive, real-time monitoring tool that offers valuable insights into tissue oxygenation and blood flow [12]. Its capacity to measure variations in oxygenated and deoxygenated hemoglobin facilitates continuous monitoring of cerebral oxygenation, which is essential for evaluating the effects of interventions such as transfusion [13, 14]. However, its clinical adoption remains uneven, particularly in low-resource settings where access to advanced monitoring technologies is limited. Many NICUs in these regions rely on empirical transfusion practices, potentially leading to over- or under-transfusion with adverse outcomes. This disparity underscores the urgent need for robust evidence on NIRS utility to inform guidelines adaptable to diverse clinical contexts, including settings without NIRS availability.

Despite the increasing interest in using NIRS to monitor neonatal outcomes, a consensus on its effectiveness in assessing improvements post-transfusion remains lacking. Studies have reported different results, with some suggested significant enhancements in cerebral oxygenation [13, 15, 16], others showed no clear benefits [17–19].

NIRS in predicting transfusion-associated complications, such as NEC, remains underexplored [20]. Yet, few studies have directly linked NIRS parameters to NEC risk stratification, leaving a critical gap in understanding how real-time oxygenation data could mitigate this devastating complication. Furthermore, conflicting findings on NIRS efficacy across studies highlight the necessity for systematic synthesis of evidence to clarify its clinical value.

The present study synthesizes evidence from existing studies to determine the effectiveness of NIRS in evaluating neonatal improvements following transfusion. By pooling data from multiple studies, we aim to provide a comprehensive understanding of the role of NIRS in this context. Additionally, this analysis will identify gaps in the current research and guide future studies to optimize the application of NIRS in neonatal care.

Method

This review followed the methodology described in the Cochrane Handbook for Systematic Reviews of Interventions [21]. The findings are reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [22]. Additionally, this review has been registered with the international database for the prospective registration of systematic reviews (PROSPERO) under ID: CRD42024596069.

Search strategy and selection criteria

We searched PubMed, Embase, and Web of Science from inception until November 2024. We searched the databases using a combination of subject terms and free words, while references of included studies were hand-searched to supplement the relevant information obtained. Detailed information on the search terms and search strategies is shown in Supplementary 1. Search results, including titles, authors, digital object identifiers (doi), and abstracts, were imported into Endnote X9 software.

Inclusion criteria

(1)Preterm infants diagnosed with anemia who required red blood cell transfusion; (2) Cerebral oxygen levels were monitored using near-infrared spectroscopy before and after transfusion.

Exclusion criteria

(1) Neonates transfused with other blood products; (2) Studies lacking specific near-infrared spectroscopy (NIRS) data; (3) Neonates with hemodynamic instability or severe congenital heart disease; (4) non-English studies, non-original studies, or studies involving non-human subjects.

The primary outcome was the changes in NIRS readings before and after transfusion. The secondary outcomes included changes in heart rate (HR), saturation of pulse oxygen (SPO_2), and hemoglobin (Hb) pre- and post-transfusion.

Data extraction and quality assessment

Data were extracted by two authors using a custom-designed form on Covidence. The extracted data included author, publication year, study area, study duration, study type, study population, sex, gestational age, age, birth weight, actual weight, transfusion volume, cerebral regional oxygen saturation ($CrSO_2$), cerebral fractional tissue oxygen extraction (cFTOE), splanchnic regional oxygen saturation ($SrSO_2$), splanchnic fractional tissue oxygen extraction (sFTOE), splanchnic-cerebral oxygenation ratio (SCOR), hemoglobin (Hb), heart rate (HR), and peripheral oxygen saturation (SpO_2).

Two researchers independently assessed quality using the Newcastle–Ottawa Scale (NOS) [23], as the Cochrane Collaboration Network recommended. In cases of disagreement, group discussions were held to reach a consensus. The NOS includes three modules assessing the study population, comparability between groups, and outcome evaluation, with eight entries scoring out of nine. A NOS score of ≥ 6 is considered indicative of high-quality literature.

Statistical analysis

Meta-analysis was conducted using Review Manager 5.4. The data collected were all continuous variables, and mean differences (MD) with 95% confidence intervals (CIs) were calculated. All variables reported as median values (including range or interquartile range) were converted to mean and standard deviation (SD) using the methodology described by J. Shi et al. [24].

The variability in effect estimates due to heterogeneity was assessed by calculating I^2 for each analysis. An I^2 value of $\geq 50\%$ indicated high heterogeneity among the study results, prompting the use of a random-effects model. Conversely, a fixed-effects model was applied when I^2 was $< 50\%$.

To evaluate the stability of the combined results for statistically significant risk factors, sensitivity analyses were performed by comparing the values obtained from both the fixed and random-effects models. Egger's test was used to assess publication bias. Differences were considered statistically significant at $P < 0.05$.

Results

Study selection

The initial search yielded 214 articles, of which 103 duplicates were removed using EndNote software. Following a review of titles and abstracts, 66 articles were excluded. A total of 45 articles were retained for full-text screening, including 9 eligible articles [13, 15, 18, 19, 25–29]. No additional eligible studies were identified through manual search. The study selection flow chart is presented in Fig. 1.

Additionally, it was noted that two studies [26, 27] originated from the same set of experiments, although they reported different types of results.

Study characteristics and quality

Nine prospective, observational studies were included, drawn from four different countries. These studies were conducted between 2008 and 2017, with sample sizes ranging from 10 to 35 infants. The studies reported specific data as follows: 8 studies provided data on $CrSO_2$, 6 studies on $SrSO_2$, 5 studies on cFTOE), 4 studies on sFTOE, 5 studies on SCOR, 5 studies on HR, 3 studies on SPO_2, and 3 studies on Hb.

Quality assessment using the Newcastle–Ottawa Scale (NOS) yielded scores indicating variability in study quality: two studies scored 6, one scored 7.5, four scored 7, one scored 8, and one achieved a score of 9 (Table 1).

Cerebral regional oxygen saturation

Eight studies reported data on $CrSO_2$. However, the values from the study by Miller et al. [25] were significantly lower than those of the other seven articles, leading to its exclusion from the meta-analysis. Consequently, seven studies were included in the meta-analysis, which revealed a significant increase in the mean difference of $CrSO_2$ following transfusion within 1–3 h.

To further analyze the data, these 7 articles were divided into two subgroups based on the degree of increase in $CrSO_2$ (below 10% or above 10%). In the subgroup with an increase below 10%, the analysis indicated a significant difference in $CrSO_2$ before and after transfusion (5 studies [18, 19, 26, 28, 29], totaling 122 infants; RR = −2.26, CI: [−3.50, −1.02], $p = 0.0003$, $I^2 = 49\%$). Similarly, in the subgroup with an increase above 10%, the change in $CrSO_2$ was found to be more pronounced before and after transfusion (2 studies [13, 15], totaling 38 infants; RR = −14.76, CI: [−18.19, −11.33], $p < 0.00001$, $I^2 = 0\%$) (Fig. 2A).

Splanchnic regional oxygen saturation

Six studies were included in the meta-analysis, which demonstrated a significantly greater mean difference in $SrSO_2$ within 1 to 3 h post-transfusion. Based on the degree of increase in $SrSO_2$ (below 20% or above 20%), these 6 articles were categorized into two subgroups for further analysis.

In the subgroup with an increase below 20%, the findings indicated a significant difference in $SrSO_2$ before and after transfusion (3 studies [18, 28, 29], totaling 63 infants; RR = −8.56, CI: [−12.67, −4.44], $p < 0.00001$, $I^2 = 17\%$) (Fig. 3B). In the subgroup with an increase above 20%, significant differences were also observed in $SrSO_2$ before and after transfusion (2 studies [13, 15], totaling 38 infants; RR = −22.79, CI: [−26.96, −18.62], $p < 0.00001$, $I^2 = 0\%$) (Fig. 2B).

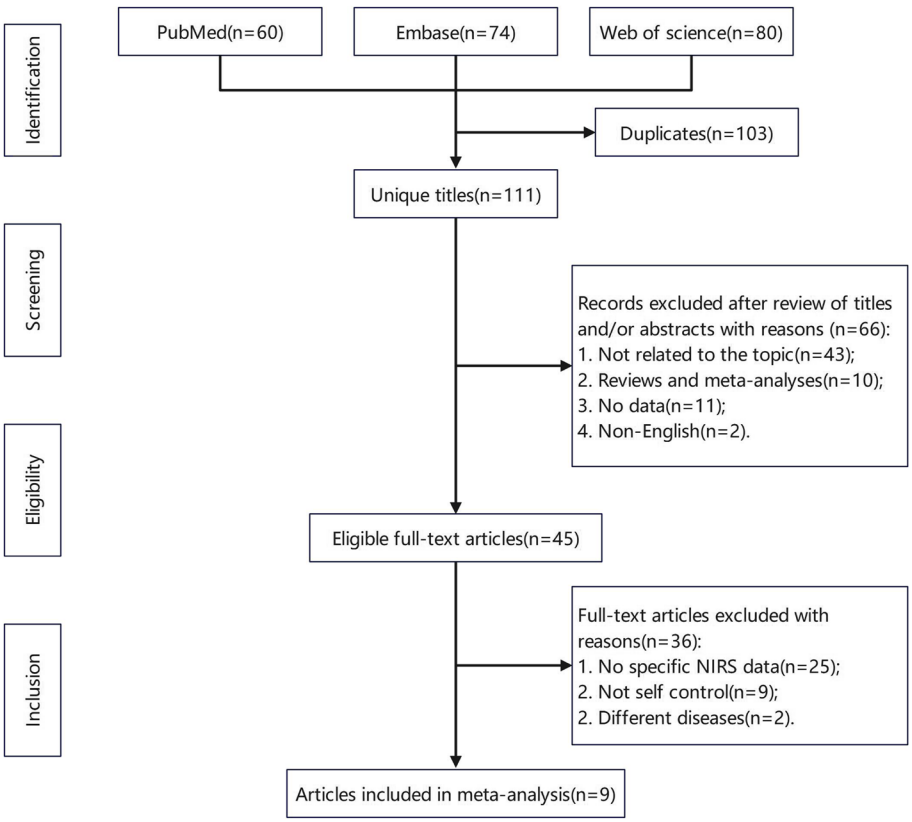


Fig. 1 PRISMA flow diagram of search process

Cerebral fractional tissue oxygen extraction

Five studies were included in the meta-analysis, indicating a significant increase in the mean difference of cFTOE before and after transfusion (5 studies [13, 15, 19, 27, 28], totaling 107 infants; RR = 0.07, CI: [0.01, 0.13], $p = 0.03$, $I^2 = 63\%$) (Fig. 2C).

Given the slightly high heterogeneity observed in the results, several factors merit consideration: (1) Different studies utilized various NIRS monitoring equipment models. (2) The methods of oxygen administration varied among pediatric patients, and the underlying medical conditions of the neonates differed across studies.

Splanchnic fractional tissue oxygen extraction

Four studies reported values for sFTOE, of which three indicated a decrease in sFTOE values after transfusion, while one reported an increase [28]. Analyzing the three studies that documented a decrease revealed a significant difference in sFTOE before and after transfusion (3 studies [13, 15, 27], totaling 67 infants; RR = 0.15, CI: [0.11, 0.19], $p < 0.00001$, $I^2 = 0\%$) (Fig. 2D).

Splanchnic-cerebral oxygenation ratio

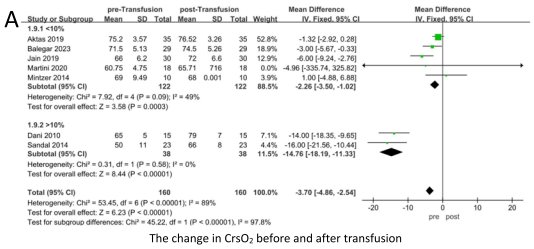
Five studies reported data on SCOR, with four indicating an increase in SCOR following transfusion and one showing a reduction [26]. Upon analyzing the findings from the four studies that reported a decrease, we found a statistically significant change in SCOR from before to after the transfusion period (4 studies [13, 15, 18, 29], totaling 91 infants; RR = −0.12, CI: [−0.17, −0.07], $p < 0.00001$, $I^2 = 0\%$) (Fig. 2E).

Hemoglobin

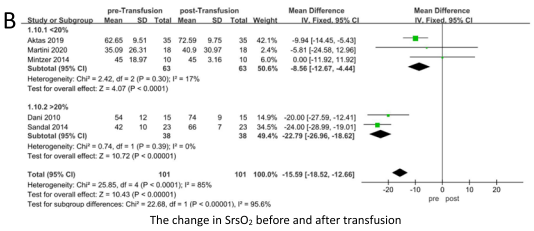
Three studies were included in the meta-analysis, indicating a significant increase in Hb mean difference after transfusion (3 studies [18, 27, 29], totaling 82 infants; RR = −2.89, CI: [−3.21, −2.57], $p < 0.00001$, $I^2 = 0\%$) (Fig. 2F).

Table 1 Study characteristics

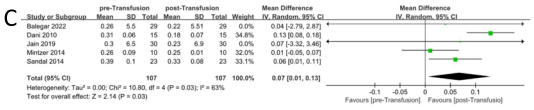
Authors	year	Study period	country	Study design	Quality score	Patients (n)	male	Gestational age(week)	Age (day)	Birth weight (g)	Actual weight(g)	transfusion volume (ml/kg)	$CrSO_2$(%)		cFTOE		$SrSO_2$(%)		sFTOE		SCOR		Hb(g/dL)		sPO_2(%)		HR(beats/min)	
													pre	post	pre	post	pre	post	pre	post	pre	post	pre	post	pre	post	pre	post
Miller et.al. (6)	2017	2010-2011	USA	prospective	7	30	17	25.5(2.1)	13.9(11.8)	768.4(241.87)		10-15	40.34(4.68)	34.89(4.85)											98.23(4.58)	97.92(0.76)	152.43(6.80)	151.89(6.62)
Sandal et.al. (6)	2014	2010-2011	Turkey	prospective	7.5	23	14	27.7(1.8)	45(14.3)	990(285)	1416(357)	15	50(11)	66(8)	0.39(0.10)	0.33(0.08)	42(10)	66(7)	0.45(0.09)	0.32(0.07)	0.64(0.28)	0.81(0.19)	8.7(2.3)					135(27)
Dani et.al. (5)	2010	2008-2009	Italy	prospective	7	15	8	27.0(2.4)		904(235)		28	63(3)	79(7)	0.31(0.06)	0.18(0.07)	54(12)	74(9)	0.43(0.11)	0.24(0.08)	0.82(0.18)	0.93(0.10)					133(8)	122(8)
Balegar et.al. (4)	2023	2014-2016	Australia	prospective	6	29	14					15	71.5(5.13)	74.5(5.26)			83.4(6.31)	83.1(6.31)			1.17(0.11)	1.12(0.09)						
Jain et.al. (4)	2019	2014-2017	USA	prospective	7	30	12	26.6(2.03)		848(270)	1008(344)	15	66(6.2)	72(6.6)	0.30(6.5)	0.23(6.9)							9.8(0.6)		95(1.6)	**95(1.8)**	138(9)	157(11)
Aktas et.al. (10)	2019	2013-2016	Turkey	prospective	7	35	13	30(2.3)	17.6(19)	1245(420)	1442(548)	15-20	75.2(3.57)	76.02(3.26)			62.65(9.51)	72.59(9.75)			0.84(0.17)	0.96(0.1)	7.94(1.40)	10.98 (1.66)			169(9.51)	155(11.89)
Balegar et.al. (5)	2022	2014-2016	Australia	prospective	6	29	14	26.7(2.03)	43(24.95)	877.7(318.91)	1512.26(599.62)	15			0.25(5.5)	0.21(5.51)			0.134(6.65)	0.131(6.65)			9.46(1.13)	12.4(1.7)				
Wintzer et.al. (5)	2014	2009-2011	USA	prospective	9	10	4	26(0)	3(0)	879(154.95)	855(120.17)	15	69(9.49)	68(0)	0.26(0.09)	0.25(0.00)	45(18.97)	45(3.16)	0.54(0.19)	0.68(0.03)					91(6.32)	91(0)	159(15.81)	157(9.49)
Martini et.al. (9)	2020	2013-2014	Italy	prospective	8	18	8	28.5(5.91)	26.36(8.85)	868(772-1198)	1066.82(297.71)	10	60.73(4.75)	65.71(7.16)			35.99(26.31)	40.9(30.97)			0.59(0.38)	0.61(0.43)	8.8(0.32)	11.63(0.80)				



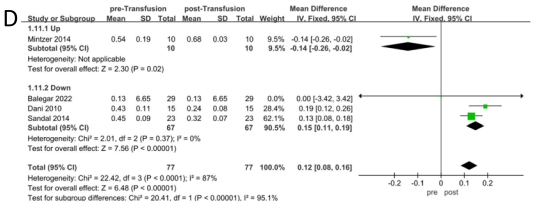
The change in $CrSO_2$ before and after transfusion



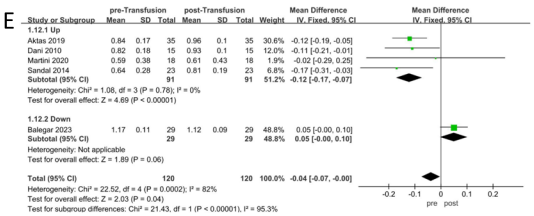
The change in $SrSO_2$ before and after transfusion



The change in cFTOE before and after transfusion

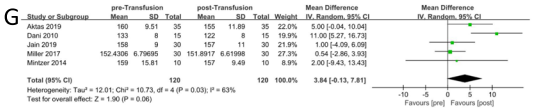


The change in sFTOE before and after transfusion

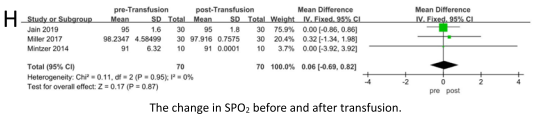


The change in SCOR before and after transfusion

The change in Hb before and after transfusion.



The change in HR before and after transfusion.



The change in SPO_2 before and after transfusion.

Fig. 2 A-H Forest map analysis before and after transfusion of $CrSO_2$, $SrSO_2$, cFTOE, sFTOE, SCOR, Hb, HR, SPO_2

Heart Rate

A total of five studies were included in the meta-analysis, indicating no significant difference in HR mean difference after transfusion (5 studies [13, 18, 19, 25, 28], totaling 120 infants; RR = 3.84, CI: [−0.13, 7.81], p = 0.06, I^2 = 63%) (Fig. 2G). Several factors may account for this outcome: (1) It is unclear whether the children in each study had mild congenital heart diseases, such as patent ductus arteriosus or patent foramen ovale; (2) It remains uncertain if the children had conditions that could affect circulation, such as sepsis or hematological disorders; (3) Changes in HR are likely attributable to a combination of factors, suggesting that an increase in blood volume alone may not be sufficient to induce a significant change in heart rate.

Saturation of pulse oxygen

Three studies [19, 25, 28] were included in the meta-analysis, which showed no significant increase in the mean difference of SpO_2 after transfusion. The analysis included a total of 70 infants (RR = 0.06, CI: [−0.69, 0.82], p = 0.87, I^2 = 0%) (Fig. 2H). It is important to note that SpO_2 is affected by various factors, including the method of oxygen administration, cardiac function, homeostasis, and the presence of underlying conditions such as pulmonary diseases, hematological disorders, or central nervous system issues. Therefore, an increase in blood volume or hemoglobin levels alone may not be sufficient to produce a significant change in oxygen saturation.

Sensitivity analysis and publication bias

We conducted sensitivity analyses on indicators with statistically significant post-transfusion differences, ensuring each had at least three included studies. For $CrSO_2$, sFTOE, SCOR, and Hb, we found that excluding any single study did not change the direction of the combined effect size, and the confidence intervals consistently excluded zero (Fig. 3 A,D,E,F). This suggests the meta-analysis results are robust and not dependent on individual studies. However, the sensitivity analysis indicated limitations in the results for $SrSO_2$ and cFTOE, as these were affected by heterogeneity and potential publication bias (Fig. 3 B,C). Large-scale, multi-center studies with standardized methods are needed to investigate the impact of blood transfusions on $SrSO_2$ and cFTOE.

Due to the limited number of included studies, the funnel plot cannot adequately reflect publication bias. Therefore, the Egger's test is used to assess publication bias in Supplementary 2. Egger's test indicated the absence of signifcant publication bias in NIRS-related indicators(P > 0.05).

Conclusion

Even with a few studies, the results still show that neonates who receive red blood cell transfusions have significant improvements in vital variables like $CrSO_2$ and

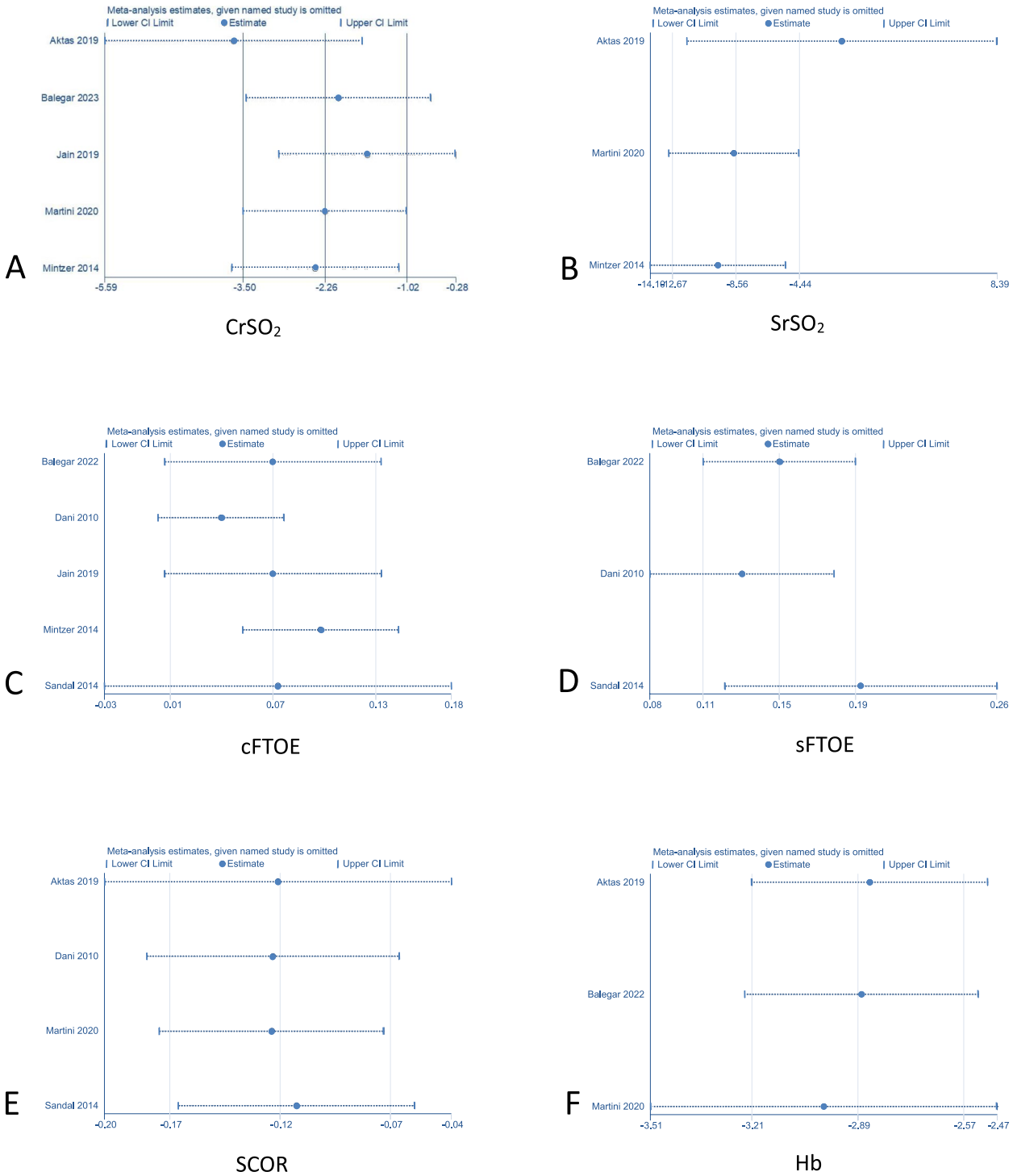


Fig. 3 A-F Sensitivity analysis of $CrSO_2$, $SrSO_2$, cFTOE, sFTOE, SCOR, Hb

$ScRO_2$, as well as calculated indices like cFTOE, sFTOE, and SCOR. Moreover, NIRS is a reliable tool for assessing the impact of red blood cell transfusions in preterm infants.

Discussion

This systematic review and meta-analysis highlights the potential of NIRS as a non-invasive monitoring tool for assessing the impact of red blood cell transfusions on

preterm infants with anemia. NIRS effectively measures improvements in oxygen delivery and perfusion post-transfusion, providing real-time data on tissue oxygenation. Increases in cerebral ($CrSO_2$) and splanchnic tissue oxygen saturation ($SrSO_2$) suggest enhanced oxygenation in critical regions, which can guide clinical decisions and optimize infant outcomes. These findings align with prior studies reporting transient increases in tissue oxygenation post-transfusion [9, 20, 23], but extend the evidence by quantifying pooled effect sizes.

Notably, the observed improvements in $CrSO_2$ and $SrSO_2$ suggest enhanced oxygen delivery to critical organs, potentially mitigating hypoxia-related complications such as neurodevelopmental impairment or NEC. This is supported by studies linking low splanchnic oxygenation to NEC risk, though our review highlights a paucity of direct evidence connecting NIRS parameters to transfusion-associated NEC outcomes-a critical gap requiring future investigation.

Contrary to expectations,HR and SpO_2 did not significantly change post-transfusion. This discrepancy may reflect differences in study populations (exclusion of hemodynamically unstable infants) or the insensitivity of systemic parameters to localized tissue oxygenation changes. The stability of SpO_2 further underscores the unique value of NIRS in detecting microcirculatory improvements undetectable by conventional monitoring.

Despite the promising results, several limitations of this study warrant consideration. Firstly, the meta-analysis included only nine prospective, observational studies, limiting the generalizability and robustness of the findings. Secondly, heterogeneity among studies, particularly in cFTOE, may stem from differences in NIRS equipment, oxygen administration methods, and neonatal conditions. Thirdly, excluding non-English studies may introduce language bias. Lastly, publication bias could not be formally assessed due to the limited number of studies.

Future research should address these limitations through larger, multi-center studies with standardized NIRS protocols and transfusion practices to confirm findings and develop robust guidelines. Research should also focus on long-term effects of transfusions, potential benefits of NIRS-guided strategies, and the applicability of NIRS in various clinical scenarios, such as acute illnesses or specific comorbidities.

While the study provides encouraging evidence for the use of NIRS in assessing transfusion impact on preterm infants, further research is essential to fully establish its clinical utility. Continued exploration of NIRS technology in neonatal care may significantly improve the management and outcomes of preterm infants with anemia.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12887-025-05731-4.

Supplementary Material 1. Search strategy.

Supplementary Material 2. The results of Egger's test.

Supplementary Material 3. Raw data.

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Authors' contributions
Both Z.S.C. and H.S. searched the databases and screened the articles. Z.S.C. extracted the data from the included articles, performed data conversion and analysis, and wrote the manuscript. H.S. polished the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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