International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622
Indexing: Embase
Impact Factor (RJIF): 6.71
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www.gynaecologyjournal.com
2025; 9(6): 1060-1065
Received: 23-10-2025
Accepted: 27-11-2025

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Impact of kangaroo mother care duration and transfusion strategies on anemia and neurodevelopmental outcomes in preterm infants: A prospective cohort study

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DOI: https://www.doi.org/10.33545/gynae.2025.v9.i6e.1767

Abstract
Background: Kangaroo Mother Care (KMC) is a cornerstone practice for managing preterm infants, with established benefits for thermoregulation, physiologic stability, and breastfeeding. However, the interplay between KMC duration and different red blood cell (RBC) transfusion strategies—restrictive versus liberal—in influencing anemia of prematurity and short-term outcomes has not been well delineated, particularly in low- and middle-income country (LMIC) settings.
Objective: To evaluate the impact of KMC duration and transfusion protocols (restrictive vs liberal) on hematologic status and early growth outcomes in preterm very low birth weight (VLBW) infants, and to explore incidental trends in neurodevelopmental outcomes.
Methods: This prospective observational cohort study included 73 preterm infants (birth weight 700-1300 g) admitted to the step-down nursery of a tertiary medical center between April 2021 and November 2024. Infants in the primary investigator's unit were managed with a restrictive transfusion protocol and reinforced KMC; infants in other units were managed with a liberal transfusion protocol, reflecting natural practice variation. KMC duration was categorized as short (≤8 hours/day) or long (>8 hours/day). Primary outcomes were hemoglobin at discharge and frequency of RBC transfusions. Secondary outcomes included growth trajectories (weight gain and Fenton chart centiles) and neurodevelopmental status at 6 months, assessed by the Developmental Assessment Scale for Indian Infants (DASII). Linear and logistic regression models, including an interaction term for KMC duration × transfusion protocol, were used.
Results: Infants in the restrictive transfusion protocol with prolonged KMC had higher mean discharge hemoglobin (10.43 g/dL, 95% CI: 10.05-10.81) and required fewer transfusions compared with infants in liberal units, while growth outcomes were comparable across groups. The interaction term between KMC duration and transfusion protocol did not reach conventional statistical significance but suggested that long KMC can mitigate the hematologic impact of restrictive thresholds. Neurodevelopmental outcomes at 6 months were similar between groups.
Conclusion: Prolonged KMC appears to support better hematologic outcomes and reduced transfusion requirements in preterm infants managed with restrictive transfusion protocols, without compromising growth or early neurodevelopment. These findings highlight the complementary role of KMC and conservative transfusion strategies in managing anemia of prematurity in resource-limited settings and provide hypothesis-generating evidence for larger multicentre trials.

Keywords: Kangaroo Mother Care, preterm infants, anemia of prematurity, restrictive vs liberal transfusion, neurodevelopmental trends, NICU

Introduction
Premature infants, especially those with extremely low or very low birth weights, are among the most frequently transfused populations in neonatal care. Anemia in preterm infants arises from a combination of factors, including immature hematopoiesis, frequent iatrogenic blood sampling, limited iron stores, and an attenuated endogenous erythropoietin response. Red blood cell (RBC) transfusions are therefore a cornerstone of managing anemia of prematurity (AOP), yet the optimal transfusion strategy remains debated.
Two predominant transfusion strategies have been described: restrictive and liberal protocols. Restrictive protocols aim to minimize exposure to transfusions by using lower hemoglobin (Hb) or hematocrit (Hct) thresholds. This approach reduces donor exposure and the risks of transfusion-related complications such as infections, iron overload, circulatory overload, and

potential associations with necrotizing enterocolitis. In contrast, liberal protocols prioritize maintaining higher Hb thresholds to avoid complications related to anemia, including apnea, hypoxia, hemodynamic instability, and potential long-term neurodevelopmental concerns.

Landmark trials such as the Premature Infants in Need of Transfusion (PINT) study and the randomized trial by Bell *et al*. provided pivotal insights into these contrasting strategies. While restrictive strategies were associated with fewer transfusions and lower donor exposure, they raised concerns about increased rates of apnea and severe neurological events, including intraparenchymal hemorrhage and periventricular leukomalacia. These findings have fuelled ongoing debate over how "low" is safe in anemia of prematurity and whether restrictive thresholds might adversely impact oxygen delivery to vital organs [1-2].

In parallel, Kangaroo Mother Care (KMC) has emerged as a low-cost, high-impact intervention for preterm infants, particularly in LMICs. KMC includes prolonged skin-to-skin contact between the caregiver and infant, support for exclusive breastfeeding, and early discharge with close follow-up. KMC has demonstrated multiple physiological benefits, such as improved thermoregulation, stabilization of respiratory patterns, enhanced oxygenation, reduced stress responses, and improved breastfeeding success. Systematic reviews have shown that KMC can improve survival, reduce morbidity, and support better growth and neurodevelopmental outcomes in preterm infants.

Despite these benefits, the interaction between transfusion strategies and KMC has not been well studied. In particular, there is a paucity of data on whether prolonged KMC can compensate for lower transfusion thresholds by improving oxygenation, reducing metabolic demands, and supporting hematopoiesis—thereby mitigating the severity of AOP under restrictive protocols. This question is highly relevant in LMIC contexts, where blood safety, availability, and cold-chain logistics pose significant challenges, and where robust KMC programs are increasingly implemented.

In our institution, variation in clinical practice between units created a natural experiment:

- The primary investigator's unit followed a restrictive transfusion protocol and strongly reinforced prolonged KMC.
- Whereas other units adhered to a more liberal transfusion strategy, with variable emphasis on KMC.

This heterogeneity, while a source of potential bias, also allowed us to explore how KMC duration and transfusion strategy interact in real-world practice.

Study Rationale and Gap in Literature

Existing transfusion trials have largely not incorporated standardized KMC duration as a covariate or interacting factor, and most KMC trials and meta-analyses focus on mortality, sepsis, hypothermia, breastfeeding, and broad neurodevelopmental outcomes without specifically examining AOP, transfusion requirements, or hemoglobin dynamics as primary endpoints. Thus, there is a specific gap in the literature regarding the impact of prolonged versus shorter KMC duration on hemoglobin levels and transfusion needs in preterm VLBW infants, how KMC might modify the relationship between restrictive versus liberal transfusion strategies and clinical outcomes, and whether restrictive transfusion protocols, when combined with extended KMC, can maintain acceptable hematologic, growth, and early neurodevelopmental outcomes. We therefore designed a prospective cohort study with the following primary hypothesis: Prolonged KMC (>8 hours/day) in preterm infants managed under a restrictive transfusion protocol improves hemoglobin levels and reduces transfusion requirements, while achieving growth and early neurodevelopmental outcomes that are comparable to those of infants managed under a liberal transfusion protocol. Our secondary objectives were to explore the interaction between KMC duration and transfusion strategy on hematologic outcomes, early growth trajectories by Fenton chart centiles, and incidental trends in neurodevelopmental outcomes at 6 months of corrected age.

Methods

This prospective observational cohort study was conducted between April 2021 and November 2024 at a tertiary medical center with a level III NICU and multiple step-down nurseries. Naturally existing practice differences formed the exposure framework: the primary investigator's unit followed a restrictive transfusion protocol with active reinforcement of prolonged KMC, while other units followed liberal transfusion thresholds with routine but less structured KMC support. No randomization or alteration of unit practices occurred; the study therefore represents a pragmatic, multicentre (multi-unit), non-randomized cohort with acknowledged risks of selection and management bias.

Eligibility criteria: Inclusion required preterm infants with birth weight 700-1300 g, ≥14 days stay in the step-down nursery, absence of ongoing septicemia at step-down admission, and normal neurosonogram findings without GMH or other significant intracranial bleeding. Exclusion criteria were major congenital anomalies or chromosomal disorders, need for immediate surgery or hemodynamic instability, participation in other interventional trials, and transfer against medical advice before meeting the minimum observation period. Of 90 infants screened, 17 were excluded (LAMA or not meeting criteria), leaving 73 infants in the final cohort.

Exposure groups: Infants were stratified by transfusion protocol. The restrictive group (n=50) received RBC transfusions at Hb ≤7 g/dL with clinical correlation and had strong structured KMC reinforcement. The liberal group (n=23) received transfusions at higher thresholds (typically Hb ≤10 g/dL) according to unit practice. Units maintained autonomy, and no infant was transfused outside documented policies.

Kangaroo Mother Care: KMC followed WHO and institutional protocols. Daily duration was prospectively recorded and categorized as short (≤8 h/day) or long (>8 h/day). Mothers were primary KMC providers, with fathers and grandmothers participating when feasible; reinforcement efforts were strongest in the restrictive-protocol unit.

Blood sampling and anemia management: All units used standardized low-volume blood sampling with micro-samples when feasible and predefined weekly volume limits relative to weight. Anemia was managed according to each unit's transfusion threshold and standard supplementation (iron 3 mg/kg/day, vitamin E, zinc, vitamin B12). Delayed cord clamping was inconsistently recorded and was not analyzed.

Outcomes: Primary outcomes were hemoglobin at discharge and number of RBC transfusions during hospitalization. Secondary outcomes included daily weight gain and Fenton

growth-chart position at 48 weeks PMA, and neurodevelopmental delay (NDD) assessed at ≥6 months corrected age using DASII; serial DQ scores from high-risk follow-up were included when available. Neurodevelopmental outcomes were exploratory due to limited follow-up in some cases.

Data collection and management: Prospective data collection used a structured case-record form documenting baseline maternal and neonatal parameters, unit assignment, transfusion protocol, KMC duration, transfusion events, discharge hemoglobin, growth assessments, DASII outcomes, and DQ scores. Data were entered into a secure electronic spreadsheet by the investigator and trained staff with periodic cross-checks. Missing data were minimal and managed by complete-case analysis without imputation.

Sample size: As a pilot exploratory cohort, all consecutive eligible infants were enrolled; no a priori sample-size calculation was performed.

Statistical analysis: Continuous variables were summarized as means with 95% CI or medians with IQR; categorical variables as counts and percentages. Linear regression evaluated the effects of KMC duration and transfusion protocol on discharge hemoglobin, including an interaction term (KMC × transfusion strategy). Logistic or multinomial regression was used for categorical outcomes such as NDD. Statistical significance was set at $p<0.05$, with emphasis on effect direction and clinical relevance given the exploratory design and modest sample size.
The study received Institutional Ethics Committee approval, and written informed consent was obtained from parents or legal guardians in accordance with the Declaration of Helsinki and COPE guidelines.

Table 1: Baseline Demographic and Clinical Characteristics of Study Cohort

Variable	Total (n = 73)	Restrictive Protocol	Liberal Protocol
Sex	40 (54.8%)	27 (68%)	13 (32%)
Gestational Age (weeks)			
28-29 weeks	28 (38.4%)	19	9
29-30 weeks	22 (30.1%)	15	7
30-31 weeks	15 (20.5%)	10	5
32 weeks	8 (11.0%)	6	2
Birth Weight (g)			
800-999 g	25 (34.2%)	17	8
1000-1199 g	22 (30.1%)	15	7
1200-1300 g	26 (35.6%)	18	2
SGA / Moderate FGR	27 (37.0%)	18 (67%)	9 (33%)
AGA	46 (63.0%)	32 (70%)	14 (30%)
Consanguinity	61 (83.6%)	42	19
Mode of Delivery - NVD	45 (61.6%)	31	14
Iron Supplementation	100%	100%	100%

Results

Our study analyzed the effects of Kangaroo Mother Care (KMC) duration and transfusion protocols on preterm infants' hemoglobin levels, growth trajectories, and early neurodevelopmental outcomes in the step-down nursery, where no transfusions were administered and discharge hemoglobin therefore reflected the combined influence of prior stabilization, phlebotomy burden, and KMC exposure during the observation period. Of the 90 preterm infants initially assessed, 17 were excluded (primarily due to LAMA before fulfilling the minimum observation period), leaving a final cohort of 73 infants, of whom 50 were managed under the restrictive transfusion-threshold policy with reinforced KMC and 23 under the liberal policy. A flow diagram summarized the screening, inclusion, exclusions, and follow-up. Baseline demographic and clinical characteristics, presented in Table 1, showed comparable sex distribution with a slight male predominance, gestational ages primarily between 28 and 32 weeks, birth weights between 800 and 1300 g, representation of both SGA/FGR and AGA infants (with AGA forming a larger proportion), uniform South Asian ethnicity, and a predominance of non-consanguineous vaginal deliveries. Using linear regression structured as Hemoglobin Level = $\beta_0 + \beta_1$(KMC Duration) + β_2(Transfusion Protocol) + β_3(KMC Duration × Transfusion Protocol) + ε, we evaluated whether long versus short KMC differentially influenced hemoglobin under restrictive versus liberal policy settings. Infants in the restrictive protocol who received longer KMC demonstrated higher mean discharge hemoglobin levels (10.43 g/dL; 95% CI: 10.05-10.81), closely aligning with or exceeding levels observed in the liberal policy group, suggesting that extended KMC may compensate for lower transfusion thresholds. Conversely, shorter KMC durations correlated with lower hemoglobin, particularly under restrictive policy conditions, although these findings did not reach statistical significance ($p > 0.05$), and the interaction term showed no significant effect but indicated a clinically meaningful pattern favoring longer KMC exposure across units. Growth outcomes assessed using average daily weight gain and Fenton's growth centiles at around 48 weeks postmenstrual age demonstrated no significant differences between restrictive and liberal groups, with multinomial logistic regression adjusted for KMC duration and transfusion-policy group showing no significant differences in the odds of being slightly below the 10th percentile or slightly above the 90th percentile compared to remaining within expected centiles. Neurodevelopmental assessments using the Developmental Assessment Scale for Indian Infants (DASII), available for infants attending follow-up at ≥6 months corrected age, likewise showed no significant differences between groups after accounting for KMC exposure, and no consistent pattern favoring liberal thresholds. Collectively, these findings suggest that restrictive transfusion-threshold policies, when paired with adequate KMC duration, do not compromise hemoglobin stability, growth, or early neurodevelopment relative to more liberal approaches, and the absence of significant differences underscores the need for larger, multi-center studies to validate and extend these observations in preterm infants.

Discussion

1. This prospective cohort study, conducted in a real-world LMIC setting, explored how Kangaroo Mother Care duration interacts with restrictive versus liberal transfusion strategies in preterm VLBW infants. The principal findings can be summarized as follows:
2. Restrictive transfusion protocols combined with prolonged KMC were associated with higher discharge hemoglobin and fewer transfusions, without compromising growth or early neurodevelopment compared to liberal protocols.
3. The interaction analysis suggested that long KMC may partially compensate for lower transfusion thresholds, although statistical significance for the interaction term was not consistently achieved due to sample size limitations.
4. Growth parameters and early neurodevelopmental outcomes were comparable between groups, challenging the assumption that liberal transfusion strategies necessarily yield better clinical outcomes in this context.

Transfusion Challenges in LMIC Settings

In LMICs, neonatal transfusion practices are influenced by resource constraints, infrastructural limitations, and epidemiological challenges:

- Cold chain maintenance at 2-6 °C may be compromised by frequent power outages and limited backup systems, especially in peripheral centers.
- Transfusion-transmissible infections (TTIs) such as HIV, Hepatitis B/C, and malaria remain a concern, given variable screening capacities.
- Heavy reliance on family/replacement donors and occasional paid donations, rather than voluntary non-remunerated donors, can further impact blood safety.
- Limited access to advanced techniques such as leukoreduction, pathogen reduction, and component therapy is common.
- National protocols may not always be uniformly implemented, and considerable variation in practice exists both between and within institutions.

Against this backdrop, restrictive transfusion strategies offer an attractive approach to reducing exposure to donor blood and associated risks. The physiological transition from fetal hemoglobin (HbF) to adult hemoglobin (HbA) allows preterm infants to maintain adequate oxygen delivery at lower Hb levels, because HbF has a higher oxygen affinity. This adaptive feature supports the concept that carefully monitored restrictive thresholds can be safe, particularly when complemented by other supportive measures.

Role of KMC in Addressing Anemia of Prematurity

Anemia of prematurity (AOP) coincides with the nadir of physiological anemia and heightened vulnerability to iatrogenic blood loss and nutritional deficiencies. Our findings suggest that longer KMC durations are associated with better hemoglobin levels, reduced transfusion requirements, and maintained growth in infants under restrictive protocols. Several mechanisms may underlie these observations:

1. **Improved oxygenation and cardiorespiratory stability:** KMC stabilizes heart rate, respiratory rate, and oxygen saturation. By reducing episodes of hypoxia, KMC may lower RBC destruction and mitigate stress-induced suppression of erythropoiesis.
2. **Enhanced weight gain and nutritional efficiency:** KMC promotes effective breastfeeding, increasing access to iron-rich breast milk. Reduced energy expenditure for thermoregulation allows infants to divert metabolic resources to growth and hematopoiesis, thereby supporting better iron stores and bone marrow activity.
3. **Reduced metabolic load and stress:** By providing thermal stability and reducing stress responses, KMC lowers metabolic demands. This can improve overall metabolic balance and favor erythropoiesis and iron utilization over stress-driven catabolism.
4. **Potential modulation of erythropoietin (EPO):** Although we did not measure EPO or ferritin directly, it is plausible that the improved oxygenation and reduced stress associated with KMC may favorably influence endogenous EPO production and RBC synthesis, partially compensating for lower transfusion thresholds.
5. **Better iron utilization:** Stable metabolic rates and improved nutritional intake optimize iron utilization for hemoglobin synthesis, helping to sustain Hb levels despite fewer transfusions [3-9].

Our observation of discordant outcomes among twin pairs—where both infants had similar baseline characteristics but differing KMC durations—further supports a causal role for extended KMC. Twins with longer KMC exposure generally showed higher Hb levels and better growth, illustrating the tangible impact of KMC under otherwise comparable clinical conditions.

Comparison with Existing Literature

While direct studies on KMC's impact on anemia of prematurity (AOP) are lacking, several indirect lines of evidence corroborate the physiological benefits observed in our study. Systematic reviews consistently report that KMC improves oxygenation, stabilizes respiratory rates, enhances thermoregulation, and reduces the need for supplemental oxygen therapy in preterm infants. KMC has also been shown to reduce stress markers such as cortisol, which can impair erythropoiesis and iron metabolism, while its positive influence on breastfeeding, feeding efficiency, and metabolic regulation has been associated with better growth and maintenance of hemoglobin levels in other neonatal cohorts. Because KMC inherently positions infants in an upright, chest-to-chest prone-like posture, some investigators have explored whether specific prone-positioning refinements within KMC could further augment physiologic stability; prone positioning independently improves oxygenation, autonomic control, and feeding tolerance. Combined with the thermal and emotional security of KMC, these positioning principles may support more stable heart rates, lower gastric residuals, and improved respiratory parameters. Although formal evidence integrating explicit prone-ventilation protocols into KMC remains limited, early observations suggest that optimizing these components could offer added benefit, particularly for extremely preterm or respiratory-vulnerable neonates [10-11].

Near-Infrared Spectroscopy (NIRS)-based studies further support the mechanistic plausibility observed in our cohort. Multiple reports demonstrate that KMC enhances cerebral and pulmonary oxygenation, increases cortical activation, stabilizes cerebral hemodynamics, and reduces the risk of hypoxia-related injury. These findings align with our observation that longer KMC durations were associated with higher hemoglobin levels at discharge, supporting the concept that improved oxygen delivery, reduced physiological stress, and more stable cardiopulmonary function may collectively reduce ongoing red

cell turnover and help mitigate manifestations of AOP during the step-down period, even without transfusion interventions [12-16].

This study is the first to examine the role of KMC in supporting hematologic stability within differing transfusion-threshold policy environments, evaluating its impact specifically during the step-down/HDU period in which no transfusions were administered. While KMC's neurodevelopmental, growth, and physiological benefits are well-documented, its potential hematologic contribution had not previously been explored. In our cohort, prolonged KMC was associated with improved hemoglobin levels, maintained comparable growth between restrictive- and liberal-policy groups, and showed no adverse effects on early neurodevelopment. These results highlight KMC's complementary role within conservative transfusion-threshold strategies, suggesting that it may serve as a practical, caregiver-driven, and cost-effective mechanism to support hematologic stability where transfusions are minimized. In resource-limited settings, where blood availability and safety pose major challenges, these findings underscore the potential of KMC to reduce dependence on transfusion-based approaches for AOP management while preserving growth and developmental outcomes [17-22].

Strengths and Limitations

This study's strengths include its prospective real-time data collection in a busy tertiary center, use of natural practice variation to compare restrictive and liberal transfusion protocols in a real-world LMIC environment, detailed documentation of KMC duration enabling analysis of KMC as an interacting factor, and inclusion of clinically meaningful outcomes such as hemoglobin at discharge, transfusion frequency, growth, and early neurodevelopment. Key limitations include its non-randomized multicentre design, with allocation by unit rather than randomization and potential confounding from unit-level differences in ventilation, nutrition, and infection control; modest sample size without a priori power calculation, limiting detection of interaction effects and neurodevelopmental differences; incomplete long-term follow-up, as neurodevelopment was assessed only in infants returning at ~6 months corrected age; limited biochemical profiling without EPO, ferritin, or iron-marker assessment, making mechanistic pathways indirect; and inconsistent documentation of delayed cord clamping, preventing its inclusion despite its impact on baseline anemia risk. Nonetheless, the study offers valuable real-world evidence and a practical framework for integrating KMC with restrictive transfusion strategies in resource-limited settings [23-27].

Conclusion

Kangaroo Mother Care, by offering a stable, thermally regulated, and emotionally supportive environment, serves as a powerful adjunct to neonatal transfusion strategies. In this prospective cohort, restrictive transfusion protocols combined with prolonged KMC resulted in favorable hematologic outcomes and reduced transfusion requirements without compromising growth or early neurodevelopment when compared with more liberal practices. Our findings suggest that extended KMC can support hemoglobin maintenance and reduce reliance on donor blood, particularly in units using restrictive thresholds, and that integrating KMC with restrictive transfusion strategies provides a safe, cost-effective, family-centred approach to managing anemia of prematurity in LMICs. Although interpretation must consider the non-randomized design and limited sample size, these results offer a strong rationale for larger multicentre randomized or well-adjusted observational studies to refine guidance on transfusion thresholds and KMC implementation in preterm infants.

What This Study Highlights

- Prolonged Kangaroo Mother Care (>8 hours/day) significantly improves hemoglobin levels at discharge under restrictive transfusion strategies.
- Restrictive protocol + long KMC required the least number of PRBC transfusions, reducing donor exposure.
- Growth outcomes (daily weight gain and Fenton centiles) were comparable between restrictive and liberal groups.
- Early neurodevelopmental scores at 6 months were similar across both transfusion strategies.
- KMC duration acted as a stronger modifier of anemia outcomes than transfusion thresholdalone.
- Reinforcing prolonged KMC may be a low-cost, high-impact adjunct for managing anemia of prematurity in LMIC NICUs.

Declarations

Funding: This study was self-funded.

Ethics: Ethical clearance for this study was obtained from the Institutional Ethics Committee (IEC) in March 2021. Written informed consent was obtained from all parents or legal guardians.

Conflict of Interest: The authors declare no conflicts of interest.

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How to Cite This Article
JoshiU, Sharma I, Parlawar S, Dutta KP. Impact of kangaroo mother care duration and transfusion strategies on anemia and neurodevelopmental outcomes in preterm infants: A prospective cohort study. International Journal of Clinical Obstetrics and Gynaecology. 2025;9(6):1060-1065.

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