

REVIEW ARTICLE

Review of Low-Cost Interventions for Reducing Neonatal Mortality and Morbidity in Low- and Middle-Income Countries

Le Thi Huynh^{1,2,3} | Hoang Thi Tran^{1,4}  | Sophie Vanhaesebrouck³

¹Neonatal Unit, Da Nang Hospital for Women and Children, Da Nang, Vietnam | ²Faculty of Nursing, Da Nang University of Medical Technology & Pharmacy, Da Nang, Vietnam | ³Department of Internal Medicine and Pediatrics, Faculty of Medicine and Health Sciences, Ghent University, Belgium and Neonatal Intensive Care Unit, University Hospitals Ghent, Ghent, Belgium | ⁴Department of Pediatrics, School of Medicine and Pharmacy, The University of Da Nang, Da Nang, Vietnam

Correspondence: Le Thi Huynh (huynhthile2526@gmail.com)

Received: 6 December 2024 | **Revised:** 21 April 2025 | **Accepted:** 6 May 2025

Funding: The authors received no specific funding for this work.

Keywords: breastfeeding | early essential newborn care | Kangaroo mother care | low-cost interventions | neonatal mortality

ABSTRACT

Aim: This review examines low-cost interventions for reducing neonatal mortality and morbidity in low- and middle-income countries (LMICs).

Methods: A systematic PubMed search and neonatal care data from World Health Organization (2014–2024) were used to revise interventions including prenatal care, early essential newborn care (EENC), resuscitation and therapeutic hypothermia, Kangaroo mother care (KMC), respiratory support, breastfeeding, sepsis prevention, safe neonatal transfer, neonatal network in LMICs and suggestions for improvement. Out of 9295 initially identified articles, 252 studies were selected as relevant to the research objectives.

Results: In LMICs, the use of antenatal corticosteroids and magnesium sulfate remains limited in routine obstetric practice. Although EENC, KMC and early breastfeeding significantly reduce neonatal mortality, these interventions are under-prioritised and insufficiently implemented. Neonatal resuscitation and respiratory support are constrained by inadequate equipment and a shortage of trained healthcare personnel. Healthcare-associated sepsis, compounded by antibiotic resistance, continues to strain neonatal intensive care units. Additionally, unsafe neonatal transfers and poor coordination among different levels of neonatal care highlight the need for better integration within regional health systems.

Conclusions: To reduce neonatal mortality and enhance care in LMICs, systematic training, effective implementation and the sustainable delivery of proven, low-cost, high-impact interventions are urgently needed.

1 | Background

The first 28 days after birth, the neonatal period, is the most vulnerable period for a child. Despite a global decline in the

neonatal mortality rate, 2.3 million newborn infants still died in 2022, according to the United Nations Inter-agency Group for Child Mortality Estimation. Most deaths occur in low-income and middle-income countries (LMICs) within the first 3 days of

Abbreviations: CPAP, continuous positive airway pressure; EENC, early essential newborn care; GBS, Group B streptococcus; KMC, Kangaroo mother care; LMICs, low-income and middle-income countries; NICU, neonatal intensive care unit; SSC, skin-to-skin contact; UNICEF, United Nations Children's Fund; WHO, World Health Organization.

Summary

- Antenatal corticosteroids and magnesium sulfate are effective but remain underused. In addition, essential newborn care practices including skin-to-skin contact, Kangaroo mother care and breastfeeding remain insufficiently implemented in low- and middle-income countries.
- Barriers such as limited equipment, staff shortages, antibiotic resistance and unsafe neonatal transfers hinder care quality.
- Systematic training and sustainable delivery of low-cost, high-impact interventions are critical to improving neonatal outcomes.

life. Common causes of death among newborns in LMICs include preterm birth and its complications, as well as neonatal infections, perinatal asphyxia and congenital anomalies [1]. Newborns dying in the neonatal period often suffer from conditions associated with a lack of quality prenatal care, care at birth, as well as treatment immediately after birth and in the first days of life. The aim of this review was to investigate low-cost interventions that could reduce neonatal morbidity and mortality rates, including prenatal, perinatal and postnatal care.

2 | Method

The authors, who are all senior neonatologists, discussed neonatal morbidity and mortality in LMICs and listed low-cost interventions to reduce these outcomes. These included prenatal care with antenatal corticosteroid and magnesium sulfate, early essential newborn care (EENC), resuscitation and therapeutic hypothermia, Kangaroo mother care (KMC), early continuous positive airway pressure (CPAP) for preterm newborns and surfactant therapy, breastfeeding, sepsis prevention, safe neonatal transfer and neonatal network care implementation. For each issue, we aimed to describe current burdens, standard recommendations for clinical practices, gaps in practices in LMICs and suggestions for improvement.

We then searched on PubMed with key words (neonatal mortality OR neonatal morbidity) AND (low-income OR middle-income countries) from 2014 to 2024. This search yielded 9295 articles. We then narrowed the results further with additional terms related to interventions using the keywords of (neonatal mortality OR neonatal morbidity) AND (low-income OR middle-income countries) AND (antenatal corticosteroids OR magnesium sulfate OR early essential newborn care OR neonatal resuscitation OR therapeutic hypothermia OR Kangaroo Mother care OR CPAP OR surfactant OR breastfeeding OR neonatal sepsis OR safe transfer OR neonatal network care). This resulted in 1594 articles. We then filtered the articles to focus on those of higher methodological quality including clinical study, clinical trial, meta-analysis, multicenter study, randomised controlled trial, review or systematic review in English language. This narrowed down the results to 592 articles. After reviewing the titles and abstracts, we identified 252 articles that were most relevant to our research topic and aligned with the

objectives of our study. We also included data from the World Health Organization related to EENC in Western Pacific Region from 2014 to 2024. The first author scanned all studies' titles and selected appropriate articles for information. The first author wrote the first draft and the other authors added information and references when needed.

3 | Results

3.1 | Prenatal Care

Caring for preterm newborn infants should start from the prenatal period onwards with the availability of routine pregnancy care and additional interventions when necessary. The WHO recommends antenatal corticosteroids for pregnant women between 24 and 34 weeks of gestation at risk of delivering within 7 days, with a repeat course if still at high risk after 7 days [2, 3]. Data from developed countries demonstrated a significant reduction in neonatal mortality rates, severe respiratory distress syndrome and intraventricular haemorrhage among preterm infants under 34 weeks of gestation who had received antenatal corticosteroids [4]. Data from LMICs also revealed a substantial decrease in intrauterine and early neonatal mortality rates with antenatal corticosteroids use, without an increase in maternal infection rates [5]. Despite these potential benefits, the routine implementation of this intervention remains low in LMICs. A WHO multicenter study on maternal and newborn health revealed significant disparities in the use of antenatal corticosteroids across nations ranging from 16% to 91%, with a median of 54% [6]. Data from eight countries in the Western Pacific region in 2018–2020 showed that only 60% of pregnant women who gave birth at 24–34 weeks of gestation received antenatal corticosteroids [7]. This highlights a substantial gap in obstetrical clinical practices in LMICs [6].

In addition to antenatal corticosteroids, magnesium sulfate is another crucial intervention recommended by the WHO for pregnant women under 32 weeks of gestation at risk of preterm birth within 24 h to prevent cerebral palsy in infants [3]. Numerous studies have demonstrated that administration of antenatal magnesium sulfate improves neonatal mortality rates, reduces intraventricular haemorrhage and decreases the incidence of cerebral palsy. Despite the growing recognition among obstetricians in recent years regarding the benefits of antenatal magnesium sulfate administration, clinical practice remains inconsistent across obstetric care units, particularly in low-resource settings [8]. Reports from nine priority countries in the Western Pacific region showed that only 28% of pregnant women delivered at before 32 weeks of gestation were given magnesium sulfate [7]. To scale up the use of antenatal corticosteroids and antenatal magnesium sulfate, updated national guidelines are essential, along with active collaboration between obstetricians and neonatologists to enhance clinical practices [3].

3.2 | Early Essential Newborn Care

The first few hours of life represent a period of critical transition for newborns, as they adapt to the extrauterine environment. However, studies have shown that approximately two-thirds of

neonatal deaths occurred within the first 3 days of life. These deaths were often preventable through simple interventions [9]. EENC has demonstrated significant effectiveness in reducing neonatal mortality and morbidity [10, 11]. It encompasses a package of evidence-based practices immediately after delivery that are recommended by the WHO. Firstly, the newborn should be thoroughly dried with a clean, dry towel within the first 30 s postpartum to prevent hypothermia and to stimulate breathing. Secondly, continuous skin-to-skin contact (SSC) between mother and infant for at least 90 min postpartum can promote thermoregulation, reduce the risk of neonatal infections and facilitate early and exclusive breastfeeding. Additional benefits include stress reduction for both mother and infant, enhanced placental expulsion and decreased maternal bleeding [12]. Delayed cord clamping until the umbilical cord pulsations cease naturally or for at least one to 3 min after birth is the third step. Delayed cord clamping has been shown to reduce the risk of anaemia in infants as well as the risk of mortality and intraventricular haemorrhages in preterm infants [13]. Finally, support is given to the mother to give early and exclusive breastfeeding to her newborn. Colostrum provides high-energy content, which prevents hypoglycaemia and hypothermia. It also contains a rich supply of antibodies and immune factors, which provide protection against infections during the neonatal period and even protect children from pneumonia later in life [14]. Breastfeeding in the first hour has been shown to significantly reduce the risk of newborn mortality in LMICs compared to feeding delayed for 2 h or longer [15]. A study from Nepal showed that EENC reduced the risk of mortality rates by 70% compared to newborns who did not receive all four components of EENC [10]. Moreover, EENC reduced admissions to the neonatal intensive care unit (NICU) by up to 30% [11].

However, the implementation of EENC has not been properly applied in many countries. Reports from nine countries of the Western Pacific Region in 2018–2020 showed that 72% of term newborns had immediate SSC, and 29% had immediate and prolonged SSC. Proportions of term newborns that had early and exclusive breastfeeding were 57% and 83%, respectively. The results for preterm and/or low birth weight newborns were even poorer: 43% had immediate SSC, 11% had immediate and prolonged SSC, 32% had early breastfeeding, and 76% had exclusive breastfeeding [7].

3.3 | Neonatal Resuscitation and Therapeutic Hypothermia

Perinatal asphyxia is the second leading cause of neonatal death, following preterm birth and its complications. While most neonates adapt well to life outside the uterus, some require assistance for stabilisation or resuscitation. Neonatal resuscitation includes thermal protection, airway clearance, positive pressure ventilation, chest compressions, endotracheal intubation and the use of medications. Depending on the condition of the neonate, some or all of these steps may be necessary for recovery. These steps must be carried out timely, accurately and with safety to ensure optimal outcomes.

Studies have shown that neonatal resuscitation practices remained suboptimal in some healthcare facilities in LMICs. For instance,

a study in Uganda found that positive pressure ventilation was initiated late due to inappropriate practices, such as excessive stimulation and suctioning of secretions [16]. Another study conducted in Vietnam found that 25% of first attempts at endotracheal intubation during neonatal resuscitation in the delivery room were unsuccessful. Furthermore, the duration of intubation was frequently longer than the recommended best practice guidelines [17]. These delays and interruptions in the initiation of positive pressure ventilation or suboptimal management during resuscitation underscored the critical need for continuous training. In addition, adequate resources should be allocated to improve the quality of neonatal resuscitation in resource-limited settings. Recent data on laryngeal mask airways have shown them to be safe for use in neonatal resuscitation by low-cadre healthcare providers, such as midwives. This subsequently provided promising options in LMICs in neonatal resuscitation [18].

Therapeutic hypothermia has been a standard of care for near-term and term newborns with moderate-to-severe hypoxic-ischemic encephalopathy in developed countries for many years; whereas in LMICs, there have been little to no differences in clinical outcomes among neonates with hypoxic-ischemic encephalopathy receiving therapeutic hypothermia or not. The discrepancy may be attributed to challenges in managing complications during cooling, such as gastric haemorrhage, pulmonary haemorrhage, infections or underlying comorbidities leading to hypoxic-ischemic encephalopathy, which contribute to increased mortality during cooling [19]. Improvements in infrastructure, management of complications and overall neonatal care are also needed to achieve optimal results. For facilities without the capability for cooling, appropriately stabilising the infant during transportation is equally important in improving the infant's prognosis. A study from Northern Vietnam showed that the use of phase change material mattresses throughout the transfer period was safe and effective. This method was also considered for implementation as an initial cooling approach, maintained throughout the transport process for facilities with limited resources, to ensure cooling occurs within 6 h of birth [20].

3.4 | KMC

Based on a meta-analysis of 345 data points from 41 countries, covering 131 296 765 live births, the estimated distribution of preterm births by gestational age group includes 84% born between 32 and 37 weeks, 10% between 28 and 32 weeks, and 5% under 28 weeks [21]. For the majority of preterm infants ≥ 32 weeks of gestation, care typically does not necessitate complex or highly technical interventions [22]. It is estimated that 75% of neonatal deaths can be prevented with effective, low-cost interventions [23]. One of these interventions is KMC, which consists of four components: prolonged SSC with the mother or a family member until the infant is full-term; exclusive breastfeeding through direct breastfeeding or other feeding methods when direct breastfeeding is not yet possible (such as through an orogastric tube, cup or spoon); close monitoring and early discharge from the hospital [22].

KMC is recommended for infants weighing < 2500 g and/or preterm infants < 37 weeks of gestation. It is a simple, effective

and low-cost intervention that can significantly improve the health outcomes of preterm infants, particularly in developing countries with limited resources [24].

KMC offers numerous benefits for as well newborns as mothers, the healthcare system and the community [3, 25]. It helps reduce hypothermia by 78% in preterm, low-birth-weight infants <2000g. Infants receiving KMC show more stable cardiopulmonary function and oxygen saturation compared to infants not receiving KMC [26]. The SSC position, with the infant lying prone on the mother's chest, head higher than the body, can help reduce gastroesophageal reflux, increase breast milk intake and prevent hypoglycemia [27]. KMC helps newborns maintain their body temperature and conserve their energy [28] and increase weight gain compared to those not receiving KMC [29]. Furthermore, it promotes mother-infant bonding, increases instinctive behaviours, makes infants more alert, stimulates the sucking reflex and timely breastfeeding, hereby increasing the rate of exclusive breastfeeding and its duration [26]. It actively involves mothers in their newborns' care and increases their self-confidence. SSC can also promote relaxation and reduce stress in mothers. By reducing the need for expensive interventions and hospital stays, KMC can also significantly lower healthcare costs and bring benefits for the healthcare system.

KMC can contribute to a significant reduction in neonatal mortality and morbidity, particularly in developing countries with limited resources [30, 31]. However, for several reasons, KMC has not been well implemented. Data from the Philippines, Colombia, Ethiopia, Bangladesh and Vietnam showed that <30%–50% of all preterm infants received KMC [25]. Data from nine priority countries in the Western Pacific Region showed that just 49% of preterm newborns under 2000g received any form of KMC, and only 10% had continuous KMC [7]. A meta-analysis of over 112 studies, with most data from 2010 to 2015 across multiple countries together with WHO data, showed that the implementation of KMC faced several barriers. The principal barriers were low maternal awareness and inadequate training and support of healthcare workers. Furthermore, KMC may also not be socially acceptable in certain cultural contexts [32].

3.5 | Enhancing Exclusive Breastfeeding

Breastfeeding stands as an optimal solution for providing nutrition to infants and young children and simultaneously serves as the most effective strategy for preventing child mortality and morbidity. It is estimated that over 800 000 deaths in children under 5 years of age could be prevented annually if breastfeeding practices were intensified across nations [33]. Abundant scientific evidence from various countries highlights the life-saving potential of breastfeeding. A 2003–2004 study in Ghana involving 10 947 newborns revealed that 16% of neonatal deaths could be prevented if infants were breastfed within the first day, with early initiation of breastfeeding within the first hour demonstrating a 22% reduction in neonatal mortality [34]. Similarly, a 2008 study of more than 22 000 mother-infant pairs in Nepal showed that early breastfeeding within 1 h after birth reduced the risk of infection-related mortality by 2–12 times compared to infants with delayed breastfeeding initiation [35]. In the immediate postpartum period, mothers often experience stress,

anxiety and a sense of insecurity following labour and delivery. Separating newborns from their mothers after birth further exacerbates stress, leading to decreased oxytocin and prolactin secretion, negatively impacting breastfeeding initiation and success. Therefore, the WHO recommends respectful care and continuous support during labour, delivery and postpartum while avoiding unnecessary mother-infant separation practices.

Supporting breastfeeding should be a continuous process initiated from prenatal consultation onwards. During the hospital stay, supporting breastfeeding includes encouragement of frequent feedings, on demand, to stimulate milk production and to meet the infant's nutritional needs. It is important to provide mothers with ongoing support, especially during the initial learning phase of breastfeeding, answering their questions, concerns and offering positive reinforcement to boost their confidence. Wherever possible, breastmilk access in the NICU needs to be enhanced by minimising separation between mothers and infants, allowing mothers to stay with their infants and breastfeed directly. Health facilities also need to support mothers with frequent milk expression and storage. For infants unable to latch directly, mothers should have access to breast pumps and should be provided with instructions on proper milk expression techniques. NICU staff should be able to maintain open communication and collaboration with mothers regarding the infant's feeding needs and the availability of breast milk. Regular updates and feedback can help mothers feel involved and supported in their breastfeeding journey.

Finally, the role of human milk banks in promoting breastfeeding needs to be highlighted. The WHO states donor human milk from human milk banks is the best alternative when the mother's own milk is not available for preterm infants [3]. Human milk banks play a crucial role in promoting breastfeeding practices beyond simply collecting, storing and distributing pasteurised breast milk. They actively engage in initiatives that encourage and support mothers to breastfeed their newborns. Human milk banks also reach out to mothers, particularly those in underserved communities in providing education and counselling on the benefits of breastfeeding as well as the importance of exclusive breastfeeding.

3.6 | Early CPAP and Surfactant for Preterm Newborns

Respiratory distress is a leading cause of admission to neonatal units, with a prevalence of over 3% among newborns and accounting for more than 50% of all the NICU admissions [36, 37]. Early diagnosis and treatment immediately after birth can help in reducing severe complications that can lead to death or long-term morbidity. Most premature infants can initiate breathing on their own, but very premature infants can quickly decompensate if not supported. Surfactant deficiency, hypothermia and hypoglycemia further increase the severity of the respiratory distress. If respiratory support is delayed until admission to a NICU, it is often less effective as alveolar micro-collapse progresses, increasing the risk of mechanical ventilation and surfactant use. Many studies have shown that providing respiratory support as soon as the newborn infant starts breathing reduced the need for oxygen, endotracheal intubation and surfactant

administration. It also reduced the rate of admission to a NICU and the risk of mechanical ventilation-related complications such as pneumonia, chronic lung disease and retinopathy of prematurity [36]. The WHO recommends that CPAP should be given to all preterm newborns with respiratory distress and that prophylactic CPAP should be considered for preterm newborns <32 weeks of gestation even without respiratory distress [3]. However, in LMICs, CPAP is often not available in delivery rooms. Nevertheless, in hospitals with high-risk pregnancies, CPAP with pressure or flow stability in delivery rooms is an essential piece of equipment for newborn care [38]. Additionally, the prone position is considered better in infants with respiratory distress because it reduces the pressure difference across the lungs between the chest and back, helps to increase ventilation uniformity and reduces hyperinflation of chest alveoli and the collapse of back alveoli as compared to the supine position. Prone positioning also reduces ventilator-associated lung injury due to over-distension of the alveoli because it improves ventilation-perfusion matching by reducing compressive pressure and increasing blood flow to the lungs in the back region. Therefore, infants with respiratory distress immediately after birth should be placed in KMC position to receive the dual benefits of both SSC and the prone position [39].

For respiratory distress syndrome in neonates, when oxygen requirement is high regardless of CPAP support, surfactant replacement therapy should be administered early to prevent progressive atelectasis, which can lead to higher oxygen requirements and the need for invasive positive pressure ventilation. Advances in clinical practice, particularly with the early initiation of CPAP, have allowed less surfactant therapy to achieve high efficacy while minimising the risks associated with invasive mechanical ventilation and ventilator-induced lung injury [40]. In parallel with CPAP support, the use of less invasive surfactant administration has gained widespread clinical adoption [41]. Other methods such as surfactant administration through laryngeal mask airway are being investigated to overcome the lack of trained personnel for intubation [42]. One important barrier for surfactant therapy in LMICs is high cost, which needs to be further tackled by several international partners.

3.7 | Prevention of Neonatal Sepsis

Neonatal sepsis is a leading cause of neonatal morbidity and mortality, particularly in preterm and low-birth-weight infants. Screening, effective management of early onset sepsis and minimising healthcare-associated sepsis risk factors in NICU are important goals in the prevention of neonatal sepsis [43].

Group B streptococcus (GBS) is a leading cause of early neonatal onset sepsis. A systematic review of 122 studies showed that the risk of early neonatal onset sepsis increased if mothers were infected or colonised with GBS. In 2015, it was estimated that 3.5 million GBS-associated preterm births occurred worldwide, with Africa accounting for 54% of estimated cases and 65% of overall perinatal deaths. The burden of GBS on LMICs is substantial [44]. Early screening and treatment of GBS-positive mothers is an efficacious approach in preventing neonatal sepsis. Nevertheless, screening programmes are predominantly implemented in developed nations, with scarce research data

from developing countries regarding maternal and neonatal infections [45]. Findings from six international studies investigating GBS screening found that both the financial burden and the high caesarean delivery rates reduce adherence to GBS screening. Therefore, in addition to implementing appropriate screening programmes, solutions to raise awareness and improve adherence are crucial to ensure effective antenatal prevention [46]. Universal screening and treatment of pregnant women with GBS vaginal infections should be implemented in routine antenatal care settings, and especially in cases of preterm prelabour rupture of membranes, antibiotic therapy should be initiated promptly upon hospital admission [47].

Healthcare-associated sepsis is the leading cause of mortality in the NICU. The incidence of late-onset sepsis in preterm infants varies from 20% to 38% within the first 120 days of life, with mortality rates ranging from 13% to 19% [48, 49]. Survivors often experience prolonged hospital stays, increased risk of necrotising enterocolitis, bronchopulmonary dysplasia and developmental delay [50].

Factors increased healthcare-associated sepsis included low birth weight, invasive interventions, prolonged use of central venous catheters, overcrowded NICU and poor hand hygiene [51]. Although non-invasive ventilation strategies help reduce lung injury and lower the incidence of ventilator-associated pneumonia, not all units are able to implement these strategies. Prolonged invasive mechanical ventilation remains a challenge in the care of extremely preterm and very low birth weight infants [52]. Delayed enteral feeding, due to poor milk tolerance, not only prolongs parenteral nutrition but also increases the risk of infection and necrotising enterocolitis [53]. Moreover, limitations in infrastructure and a lack of coordination between obstetric and paediatric specialties increase the isolation of high-risk infants in intensive care units, causing a missed opportunity for early breast milk exposure.

There are many important strategies for healthcare-associated sepsis prevention and management that should be focused on. Ensuring strict hand hygiene practices among NICU staff is the most effective measure to prevent healthcare-associated infections. Ongoing training and monitoring are essential to maintaining high standards [54]. Promoting practices that reduce mother-infant separation, such as EENC, helps lower NICU admissions and reduces unnecessary antibiotic use, benefiting both infant health and healthcare efficiency [11]. Establishing clear criteria for NICU admissions based on the level of care needed helps manage overcrowding. Rational space allocation allows for better mother-infant bonding, which supports breastfeeding and reduces healthcare strain [25]. Adhering to aseptic procedures, using checklists and closely monitoring intravenous lines are crucial for preventing infections and ensuring proper care during medical interventions [55]. Antibiotic resistance is also an issue that contributes to the difficulty in controlling sepsis in the NICU. The prolonged use of broad-spectrum antibiotics over the past decades has contributed to the increase in multi-drug-resistant Gram-negative bacteria, raising the risk of neonatal mortality [56]. Rational use of antibiotics is very important in clinical practice, including the appropriate selection of initial antibiotics and stopping antibiotics immediately once the course is completed or if there is no evidence of infection.

Using antibiotics based on blood culture results helps reduce overuse and resistance. Effective antibiotic stewardship minimises the risks of multidrug-resistant infections and reduces treatment costs [57].

3.8 | Safe Transfer Is a Critical Component of Neonatal Care

While prenatal transfer is the safest mode of transfer for newborns, postpartum transfers also occur when a facility is inadequately equipped to manage the newborns' medical condition. Unsafe transfers significantly contribute to worsening outcomes, increasing the risk of mortality and morbidity [58].

A study conducted in a tertiary care centre in North India identified the most common problems encountered during neonatal transport to be hypothermia, shock and the need for cardiopulmonary resuscitation. This study also reported a mortality rate exceeding 30%, with over half of these deaths occurring within the first 24 h after transferring. Mortality was directly linked to issues arising before, during and after the transport process [59]. Another study of 552 neonates transferred from peripheral hospitals to a tertiary hospital in Southern Vietnam revealed that 14 infants (2.5%) experienced cardiac arrest prior to admission, with the leading cause being endotracheal tube displacement during the transfer. Additionally, 24.2% of infants went into shock within 12 h of admission to NICU. The mortality rate was still significantly high, accounting for 23.5% of the total [60].

Challenges and consequences of unsafe transfers are numerous. Firstly, there is often a lack of appropriate transfer vehicles and a shortage of skilled personnel to handle transport-related emergencies. This leads to unprepared quick transfers hindering proper stabilisation before and during the transfer journey. Secondly, monitoring and recording abnormal events throughout the transfer process is often neglected. Thirdly, poor communication and collaboration are common. Inadequate inter-facility communication and the absence of adequate specialised support compromise the professionalism of the healthcare team. By focusing on these challenges, a healthcare system can and should be created for safe transfers, ensuring that every newborn receives the most optimal care.

If an emergency delivery precludes prenatal transfer, infants should be transferred postnatally when the facility exceeds its treatment capabilities, ensuring, however, initial stabilisation. Mothers and infants should be transferred together. Maintaining stable blood glucose, temperature, respiratory and circulatory stability, performing laboratory tests and providing family support is the key to safe patient transfer. Maintaining stable infant thermoregulation during transfer is crucial. If the infant requires respiratory support or intravenous fluids during transfer, a transport incubator is the appropriate equipment. However, modern transport incubators are not widely available, especially in LMICs, making SSC with the mother or a caregiver a safe and effective method for preventing hypothermia in infants. These practices are recommended by the WHO and currently practised by many district and provincial hospitals during transfers in LMICs [3]. Safe and stable transfer following resuscitation is an integral component of neonatal care, minimising

adverse events during transport and optimising outcomes for neonates. By adhering to established transfer principles, maintaining open communication between sending and receiving units, and using effective thermoregulation strategies, we can ensure that every infant receives the safest and most effective care during transfer, maximising their chances of survival and limitation of complications.

3.9 | Establishing Geographically Distributed Neonatal Care Networks

A geographically distributed neonatal care network serves as an organisational framework for implementing and operating comprehensive neonatal care services. The establishment of such a network within each country's region depends on various factors, including geographical characteristics, socioeconomic conditions and the level of healthcare infrastructure development. Healthcare models in LMICs are typically structured according to a pyramid model, with primary care facilities at the base, followed by secondary and tertiary care facilities at ascending levels. Clinical practice has highlighted the lack of organisational support among healthcare facilities in terms of neonatal care unit organisation, specialised issues in neonatal disease management and the absence of communication and support when infants require transfer from basic care units to specialised units to ensure safe transfer [61].

4 | Discussion

There are gaps that need to be addressed to reduce neonatal mortality and morbidity in LMICs. Establishing a regional neonatal care network is crucial to improve the quality of neonatal care. This involves creating a formal neonatal network, with neonatal units in tertiary hospitals acting as the network leaders. These tertiary hospitals would be responsible for developing and implementing standardised clinical guidelines for managing common neonatal conditions, ensuring consistency and quality across the country. In addition, neonatal guidelines must be adapted to suit all levels of care in the country. Tertiary hospitals should provide frequent support to maintain safe prenatal and neonatal transfers. This includes ensuring clear communication before and during transportation, offering feedback and conducting regular training and education for healthcare professionals. These efforts would enhance the skills and competencies of healthcare providers, particularly in local units. Monitoring and supervision should be based on data related to neonatal morbidity and mortality, with regular visits or online meetings with local hospitals becoming common practice.

Continuous education and training for all healthcare providers involved in maternal and neonatal care are essential for the successful implementation of EENC, KMC, resuscitation practices, infection control and rational antibiotic use. Furthermore, raising awareness among the community about the importance of EENC, KMC and breastfeeding is crucial. Encouraging families to adopt these practices for their newborns can lead to improved neonatal outcomes. Dispelling myths and misconceptions surrounding breastfeeding is an important part of improving neonatal care. Addressing common breastfeeding challenges faced

by mothers can also make a significant difference. In some cultural contexts, practices like KMC may not be socially acceptable. Addressing these barriers is vital for the success of neonatal care interventions.

Improving the quality of neonatal resuscitation is another key strategy. This includes ensuring the availability of neonatal resuscitation algorithms at each level of care, coupled with appropriate training and equipment. Providing post-resuscitation care based on the condition of the neonate is also essential. Resuscitation algorithms must be integrated into the EENC to avoid conflicting guidelines and practices. The use of early CPAP, appropriate surfactant therapy for preterm neonates with respiratory distress syndrome, and cooling therapy for HIE should also be implemented while the need for low-cost equipment such as cooling machines, respiratory support machines, surfactant and monitoring devices is essential in LMICs.

This review highlights cost-effective and feasible interventions for resource-limited settings. Data on the burden of main causes of neonatal morbidity and mortality and gaps in clinical practices in LMICs were available for some topics but not all. Although randomised controlled trials are considered the gold standard, they are challenging to implement in resource-limited settings, so data for randomised controlled trials among clinical practices in LMICs were not widely available. Studies to describe the challenges in the implementation of EENC, KMC, therapeutic hypothermia, early CPAP or surfactant have been limited. Studies on inventions of low-cost equipment such as cooling machines, ventilators, non-invasive monitoring or drugs such as surfactant were also scarce. Furthermore, monitoring and evaluation mechanisms are often inadequate, making it difficult to assess the true effectiveness of interventions across diverse contexts.

5 | Conclusion

Neonatal mortality and morbidity is a critical burden in LMICs because of various challenges in the implementation of effective measures. A suitable framework for low-cost interventions focusing on prenatal care, EENC and resuscitation, KMC, breastfeeding, early CPAP for preterm newborns, sepsis prevention, safe transfer and regional neonatal network should be implemented for improving the quality of neonatal care. Raising awareness among mothers and family through training programs will promote EENC, KMC and breastfeeding. Healthcare providers play a key role in supporting mothers and newborns before and after birth as well as in NICU settings to ensure infants receive optimal nutrition and care; therefore, transfer of knowledge and training of healthcare workers is important in achieving this goal.

Author Contributions

Le Thi Huynh: conceptualization, writing – original draft, methodology, writing – review and editing, resources, data curation, project administration. **Hoang Thi Tran:** conceptualization, writing – review and editing, data curation, methodology, supervision. **Sophie Vanhaesebrouck:** methodology, supervision, writing – review and editing, data curation, conceptualization.

Conflicts of Interest

The authors declare no conflicts of interest.

References

1. UNICEF, “Neonatal Mortality,” (2023), <https://data.unicef.org/topic/child-survival/neonatal-mortality/>.
2. F. Althabe, J. M. Belizán, E. M. McClure, et al., “A Population-Based, Multifaceted Strategy to Implement Antenatal Corticosteroid Treatment Versus Standard Care for the Reduction of Neonatal Mortality due to Preterm Birth in Low-Income and Middle-Income Countries: The ACT Cluster-Randomised Trial,” *Lancet* 385, no. 9968 (2015): 629–639, [https://doi.org/10.1016/S0140-6736\(14\)61651-2](https://doi.org/10.1016/S0140-6736(14)61651-2).
3. World Health Organization, “Recommendations for Care of the Preterm or Low-Birth-Weight Infant,” (2022), WHO.
4. R. Vidavalur, Z. Hussain, and N. Hussain, “Association of Survival at 22 Weeks’ Gestation With Use of Antenatal Corticosteroids and Mode of Delivery in the United States,” *JAMA Pediatrics* 177, no. 1 (2023): 90–93.
5. O. T. Oladapo, J. P. Vogel, G. Piaggio, et al., “Antenatal Dexamethasone for Early Preterm Birth in Low-Resource Countries,” *New England Journal of Medicine* 383, no. 26 (2020): 2514–2525, <https://doi.org/10.1056/NEJMoa2022398>.
6. J. P. Vogel, J. P. Souza, A. M. Gülmezoglu, et al., “Use of Antenatal Corticosteroids and Tocolytic Drugs in Preterm Births in 29 Countries: An Analysis of the WHO Multicountry Survey on Maternal and Newborn Health,” *Lancet* 384, no. 9957 (2014): 1869–1877.
7. World Health Organization Western Pacific Region, *Third Biennial Progress Report: 2018–2020 (Action Plan for Health Newborn Infants in the Western Pacific Region: 2014–2020)* (WHO Regional Office for the Western Pacific, 2022), 2022.
8. E. S. Shepherd, S. Goldsmith, L. W. Doyle, et al., “Magnesium Sulphate for Women at Risk of Preterm Birth for Neuroprotection of the Fetus,” *Cochrane Database of Systematic Reviews* 5, no. 5 (2024): Cd004661.
9. World Health Organization, “Action Plan for Healthy Newborn Infants in the Western Pacific Region,” (2014–2020), <https://iris.wpro.who.int/handle/10665/10454>.
10. E. Bryce, L. C. Mullany, S. K. Khatri, J. M. Tielsch, S. C. LeClerq, and J. Katz, “Coverage of the WHO’S Four Essential Elements of Newborn Care and Their Association With Neonatal Survival in Southern Nepal,” *BMC Pregnancy and Childbirth* 20, no. 1 (2020): 540.
11. H. T. Tran, P. Mannava, J. C. S. Murray, et al., “Early Essential Newborn Care Is Associated With Reduced Adverse Neonatal Outcomes in a Tertiary Hospital in Da Nang, Viet Nam: A Pre- Post- Intervention Study,” *EClinicalMedicine* 6 (2018): 51–58.
12. E. R. Moore, N. Bergman, G. C. Anderson, and N. Medley, “Early Skin-To-Skin Contact for Mothers and Their Healthy Newborn Infants,” *Cochrane Database of Systematic Reviews* 11, no. 11 (2016): Cd003519.
13. H. Rabe, G. M. Gyte, J. L. Díaz-Rossello, and L. Duley, “Effect of Timing of Umbilical Cord Clamping and Other Strategies to Influence Placental Transfusion at Preterm Birth on Maternal and Infant Outcomes,” *Cochrane Database of Systematic Reviews* 9, no. 9 (2019): Cd003248.
14. A. W. A. Nasuf, S. Ojha, and J. Dorling, “Oropharyngeal Colostrum in Preventing Mortality and Morbidity in Preterm Infants,” *Cochrane Database of Systematic Reviews* 9 (2018): CD011921.
15. Group NS, “Timing of Initiation, Patterns of Breastfeeding, and Infant Survival: Prospective Analysis of Pooled Data From Three Randomised Trials,” *Lancet Global Health* 4, no. 4 (2016): e266–e275.
16. D. Helldén, S. Myrner Hög, N. J. Pejovic, et al., “Neonatal Resuscitation Practices in Uganda: A Video Observational Study,” *BMJ Paediatrics Open* 5, no. 1 (2021): e001092.

17. T. Dempsey, H. T. Nguyen, H. L. Nguyen, et al., "Endotracheal Intubation Performance at a Large Obstetric Hospital Delivery Room, Hanoi, Vietnam," *Resuscitation Plus* 12 (2022): 100338, <https://doi.org/10.1016/j.resplu.2022.100338>.
18. N. J. Pejovic, S. Myrnerets Höök, J. Byamugisha, et al., "A Randomized Trial of Laryngeal Mask Airway in Neonatal Resuscitation," *New England Journal of Medicine* 383, no. 22 (2020): 2138–2147.
19. D. Mascarenhas, M. Goyal, R. Nanavati, S. B. Kirthana, and S. Subhadarsini, "Short-Term Outcome and Complications of Therapeutic Hypothermia in Neonates With Moderate-To-Severe Hypoxic Ischaemic Encephalopathy: A Single-Centre Retrospective Observational Study in a Hospital in Mumbai, India," *Paediatrics and International Child Health* 42, no. 3–4 (2022): 117–126.
20. H. T. T. Tran, D. M. Tran, H. T. Le, L. Hellström-Westas, T. Alfvén, and L. Olson, "Cooling During Transportation of Newborns With Hypoxic Ischemic Encephalopathy Using Phase Change Material Mattresses in Low-Resource Settings: A Randomized Controlled Trial in Hanoi, Vietnam," *BMC Pediatrics* 24, no. 1 (2024): 509, <https://doi.org/10.1186/s12887-024-04987-6>.
21. H. Blencowe, S. Cousens, M. Z. Oestergaard, et al., "National, Regional, and Worldwide Estimates of Preterm Birth Rates in the Year 2010 With Time Trends Since 1990 for Selected Countries: A Systematic Analysis and Implications," *Lancet* 379, no. 9832 (2012): 2162–2172.
22. Organization WH, "Introducing and Sustaining EENC in Hospitals: Kangaroo Mother Care for Pre-Term and Low-Birthweight Infants," accessed April 24, 2020, <https://iris.wpro.who.int/handle/10665/14166>.
23. C. P. Howson, M. V. Kinney, L. McDougall, and J. E. Lawn, "Born Too Soon: Preterm Birth Matters," *Reproductive Health* 10, no. Suppl 1 (2013): S1.
24. S. Arya, H. Naburi, K. Kawaza, et al., "Immediate 'Kangaroo Mother Care' and Survival of Infants With Low Birth Weight," *New England Journal of Medicine* 384, no. 21 (2021): 2028–2038.
25. Organization WH, "Kangaroo Mother Care Implementation Strategy for Scale-Up Adaptable to Different Country Contexts," (2023), WHO.
26. E. O. Boundy, R. Dastjerdi, D. Spiegelman, et al., "Kangaroo Mother Care and Neonatal Outcomes: A Meta-Analysis," *Pediatrics* 137, no. 1 (2016): e20152238.
27. D. Pandya, G. A. P. Kartikeswar, G. Patwardhan, S. Kadam, A. Pandit, and S. Patole, "Effect of Early Kangaroo Mother Care on Time to Full Feeds in Preterm Infants - A Prospective Cohort Study," *Early Human Development* 154 (2021): 105312.
28. K. Chi Luong, T. Long Nguyen, D. H. Huynh Thi, H. P. Carrara, and N. J. Bergman, "Newly Born Low Birthweight Infants Stabilise Better in Skin-To-Skin Contact Than When Separated From Their Mothers: A Randomised Controlled Trial," *Acta Paediatrica* 105, no. 4 (2016): 381–390.
29. D. Sharma, N. Farahbakhsh, S. Sharma, P. Sharma, and A. Sharma, "Role of Kangaroo Mother Care in Growth and Breast Feeding Rates in Very Low Birth Weight (VLBW) Neonates: A Systematic Review," *Journal of Maternal-Fetal and Neonatal Medicine* 32, no. 1 (2017): 129–142.
30. D. Sharma, S. Murki, and O. T. Pratap, "To Compare Growth Outcomes and Cost-Effectiveness of 'Kangaroo Ward Care' With 'Intermediate Intensive Care' in Stable Extremely Low Birth Weight Infants: Randomized Control Trial," *Journal of Maternal-Fetal & Neonatal Medicine* 30, no. 14 (2017): 1659–1665.
31. S. Sivanandan and M. J. Sankar, "Kangaroo Mother Care for Preterm or Low Birth Weight Infants: A Systematic Review and Meta-Analysis," *BMJ Global Health* 8, no. 6 (2023): e010728, <https://doi.org/10.1136/bmjgh-2022-010728>.
32. G. J. Chan, A. S. Labar, S. Wall, and R. Atun, "Kangaroo Mother Care: A Systematic Review of Barriers and Enablers," *Bulletin of the World Health Organization* 94, no. 2 (2016): 130–141j, <https://doi.org/10.2471/BLT.15.157818>.
33. C. G. Victora, R. Bahl, A. J. Barros, et al., "Breastfeeding in the 21st Century: Epidemiology, Mechanisms, and Lifelong Effect," *Lancet* 387, no. 10017 (2016): 475–490.
34. K. M. Edmond, C. Zandoh, M. A. Quigley, S. Amenga-Etego, S. Owusu-Agyei, and B. R. Kirkwood, "Delayed Breastfeeding Initiation Increases Risk of Neonatal Mortality," *Pediatrics* 117, no. 3 (2006): e380–e386.
35. L. C. Mullany, J. Katz, Y. M. Li, et al., "Breast-Feeding Patterns, Time to Initiation, and Mortality Risk Among Newborns in Southern Nepal," *Journal of Nutrition* 138, no. 3 (2008): 599–603, <https://doi.org/10.1093/jn/138.3.599>.
36. E. E. Foglia, E. A. Jensen, and H. Kirpalani, "Delivery Room Interventions to Prevent Bronchopulmonary Dysplasia in Extremely Preterm Infants," *Journal of Perinatology* 37, no. 11 (2017): 1171–1179.
37. N. Switchenko, V. Shukla, M. Mwenenchanya, et al., "Neonatal Respiratory Support Utilization in Low- and Middle-Income Countries: A Registry-Based Observational Study," *Neonatology* 121, no. 1 (2024): 116–124.
38. B. Jonsson, T. Drevhammar, and S. Donaldsson, "Function of Neonatal CPAP Systems and the Importance of Total Flow," *Pediatric Pulmonology* 58, no. 1 (2023): 18–19.
39. Y. Kato, A. Takemoto, C. Oumi, et al., "Effects of Skin-To-Skin Care on Electrical Activity of the Diaphragm in Preterm Infants During Neurally Adjusted Ventilatory Assist," *Early Human Development* 157 (2021): 105379.
40. P. Reynolds, P. Bustani, C. Darby, et al., "Less-Invasive Surfactant Administration for Neonatal Respiratory Distress Syndrome: A Consensus Guideline," *Neonatology* 118, no. 5 (2021): 586–592.
41. J. A. Gallup, S. M. Ndakor, C. Pezzano, and J. M. B. Pinheiro, "Randomized Trial of Surfactant Therapy via Laryngeal Mask Airway Versus Brief Tracheal Intubation in Neonates Born Preterm," *Journal of Pediatrics* 254 (2023): 17–24.e2.
42. R. C. Silveira, C. Panceri, N. P. Munõz, M. B. Carvalho, A. C. Fraga, and R. S. Procianny, "Less Invasive Surfactant Administration Versus Intubation-Surfactant-Extubation in the Treatment of Neonatal Respiratory Distress Syndrome: A Systematic Review and Meta-Analyses," *Jornal de Pediatria* 100, no. 1 (2024): 8–24.
43. C. Fleischmann, F. Reichert, A. Cassini, et al., "Global Incidence and Mortality of Neonatal Sepsis: A Systematic Review and Meta-Analysis," *Archives of Disease in Childhood* 106, no. 8 (2021): 745–752.
44. A. C. Seale, F. Bianchi-Jassir, N. J. Russell, et al., "Estimates of the Burden of Group B Streptococcal Disease Worldwide for Pregnant Women, Stillbirths, and Children," *Clinical Infectious Diseases* 65, no. suppl_2 (2017): S200–S219, <https://doi.org/10.1093/cid/cix664>.
45. G. J. Chan, A. C. Lee, A. H. Baqui, J. Tan, and R. E. Black, "Prevalence of Early-Onset Neonatal Infection Among Newborns of Mothers With Bacterial Infection or Colonization: A Systematic Review and Meta-Analysis," *BMC Infectious Diseases* 15 (2015): 118.
46. S. Pangerl, D. Sundin, and S. Geraghty, "Group B Streptococcus Screening Guidelines in Pregnancy: A Critical Review of Compliance," *Maternal and Child Health Journal* 25, no. 2 (2021): 257–267.
47. J. Y. Mei and N. S. Silverman, "Group B Streptococcus in Pregnancy," *Obstetrics and Gynecology Clinics of North America* 50, no. 2 (2023): 375–387.
48. M. H. Tsai, J. F. Hsu, S. M. Chu, et al., "Incidence, Clinical Characteristics and Risk Factors for Adverse Outcome in Neonates With Late-Onset Sepsis," *Pediatric Infectious Disease Journal* 33, no. 1 (2014): e7–e13.
49. R. G. Greenberg, S. Kandefer, B. T. Do, et al., "Late-Onset Sepsis in Extremely Premature Infants: 2000–2011," *Pediatric Infectious Disease Journal* 36, no. 8 (2017): 774–779.

50. P. Korček, Z. Korčeková, I. Berka, J. Kučera, and Z. Straňák, "Corpus Callosum Growth and Neurodevelopmental Outcome Are Negatively Influenced by Systemic Infection in Very Low-Birth-Weight Infants," *Journal of Child Neurology* 36, no. 10 (2021): 883–887.
51. H. Attia Hussein Mahmoud, R. Parekh, S. Dhandibhotla, et al., "Insight Into Neonatal Sepsis: An Overview," *Cureus* 15, no. 9 (2023): e45530.
52. V. V. Ramaswamy, R. Devi, and G. Kumar, "Non-Invasive Ventilation in Neonates: A Review of Current Literature," *Frontiers in Pediatrics* 11 (2023): 1248836.
53. J. R. Swanson, A. Becker, J. Fox, et al., "Implementing an Exclusive Human Milk Diet for Preterm Infants: Real-World Experience in Diverse NICUs," *BMC Pediatrics* 23, no. 1 (2023): 237.
54. P. Rakshit, N. Nagpal, S. Sharma, K. Mishra, A. Kumar, and T. Banerjee, "Effects of Implementation of Healthcare Associated Infection Surveillance and Interventional Measures in the Neonatal Intensive Care Unit: Small Steps Matter," *Indian Journal of Medical Microbiology* 44 (2023): 100369.
55. M. Van Rens, K. Hugill, M. A. K. Gaffari, et al., "Outcomes of Establishing a Neonatal Peripheral Vascular Access Team," *Archives of Disease in Childhood. Fetal and Neonatal Edition* 108, no. 1 (2023): 88–89.
56. K. Sands, M. J. Carvalho, E. Portal, et al., "Characterization of Antimicrobial-Resistant Gram-Negative Bacteria That Cause Neonatal Sepsis in Seven Low- and Middle-Income Countries," *Nature Microbiology* 6, no. 4 (2021): 512–523.
57. C. Wattal, N. Kler, J. K. Oberoi, A. Fursule, A. Kumar, and A. Thakur, "Neonatal Sepsis: Mortality and Morbidity in Neonatal Sepsis due to Multidrug-Resistant (MDR) Organisms: Part 1," *Indian Journal of Pediatrics* 87, no. 2 (2020): 117–121.
58. M. M. Gray, T. Riley, N. D. Greene, et al., "Neonatal Transport Safety Metrics and Adverse Event Reporting: A Systematic Review," *Air Medical Journal* 42, no. 4 (2023): 283–295.
59. J. Singh, P. Dalal, G. Gathwala, and R. Rohilla, "Transport Characteristics and Predictors of Mortality Among Neonates Referred to a Tertiary Care Centre in North India: A Prospective Observational Study," *BMJ Open* 11, no. 7 (2021): e044625.
60. N. T. K. Nhi and L. A. Pham, "Evaluation of the Score for Neonatal Acute Physiology Extension II and Addition Factors in Neonatal Intensive Care Unit," *Ho Chi Minh City Journal of Medicine* 23, no. 4 (2019): 168–173.
61. K. Kalaris, G. Wong, and M. English, "Understanding Networks in Low- and Middle-Income Countries' Health Systems: A Scoping Review," *PLOS Global Public Health* 3, no. 1 (2023): e0001387.