

New WHO Recommendations for the Care of Preterm and Low Birth Weight Infants – A Potential Strategy to Transform the Current Healthcare Needs of Neonates

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Despite major advances in the field of maternal and child health, preterm and lowbirth neonates still carry a substantial burden of both mortality and morbidity, especially in low and middle-income countries. In view of accumulating new evidence, there was a felt need for updating and expanding the previous World Health Organization recommendations of 2015. The new evidence-based recommendations for care of the preterm or low birthweight infant consist of 25 recommendations and one good practice statement and were published on 15 November, 2022. We herein provide the key recommendations for the benefit of the readers.

Keywords: Management, Small vulnerable newborns.

The overall needs of preterm and low birth weight neonates with respect to their requirement of resuscitation, respiratory support, nutrition, and long-term neurodevelopmental follow-up are remarkably different from term born neonates [1-3]. Taking into consideration the burden of global mortality, preterm account for 36.1% of total neonatal deaths and 17.7% of death under 5 years of age [4].

The WHO Departments of Maternal, Newborn, Child and Adolescent Health and Ageing (MCA) and Sexual and Reproductive Health and Research (SRH) had developed various guidelines based on the available evidence in 2011, 2012 and 2015 [5-7]. Since the last guidelines, significant evidence has emerged in numerous areas of neonatal health that could potentially serve to simplify and improve the complexities associated with the care of small and sick neonates. In 2020, a group of experts comprising 25 Guideline Development Group (GDG) members from six WHO regions examined and interpreted the evidence, formulated the final recommendations, and provided the related comments at multiple virtual meetings between November, 2021 and January, 2022. On November 15, 2022, WHO published the outcomes of this process in the ‘WHO Recommendations for Care of the Preterm or Low Birthweight Infant [8].’

The guidelines provide insight into the implementation aspect of these recommendations in the care of small and sick neonates along with addressing other associated applicability issues. A detailed description of the need for

focusing on future implications has also been included. Lastly, the monitoring and evaluation of the impact of these guidelines to inform and update the future guidelines has also been taken into account.

Target audience: Prioritizing neonatal health with the aim to end preventable deaths, the guidelines intended to update the recommendations that would immensely impact the areas with high clinical or public health burden. For fulfilling the objective, the guidelines focused to inform the national and subnational public health policy-makers, implementers and managers of maternal, newborn and child health programs, supervisors for in-service training, health workers, NGOs, professional societies, researchers, and those involved in the education of parents.

Guideline development methods: The Grading of Recommendation Assessment, Development and Evaluation (GRADE) approach was used to define the quality of evidence and strength of quantitative evidence, whereas the GRADE-CERQual (Confidence in the Evidence from Reviews of Qualitative Research) tool was used for qualitative evidence. The DECIDE approach (Developing and Evaluating Communication strategies to support Informed Decisions and practice based on Evidence), an evidence-to-decision tool, was used to formulate the recommendations by the GDG members.

The Concept of Family Values and Preferences

Being cognizant of the interventions to improve the survival of vulnerable preemies and taking into consideration

the growing awareness among parents about the care of small and sick neonates, the WHO committee reviewed 203 studies from Low- and middle-income countries (LMICs) about 'what matters' to families with regard to the care of preterm and LBW neonates. The committee reported that families aspire for the best possible positive outcome for their babies, urge to be involved as an active care provider and have the desire to participate in decision making related to interventions provided to their babies. The domains covered under family values and preferences include- positive outcomes, active involvement in care, coping at home, emotional support for the family, health-care environment, information needs met, logistic support and positive relationships with staff.

RECOMMENDATIONS

The recommendations were based not only on the concept of the 'assessment of effects' that includes benefits and harms of the interventions and preterm and LBW infant health outcomes, but has also taken into consideration the values and preferences of the families and health workers, acceptability, resource requirements, feasibility and equity. Seventeen new systematic reviews were commissioned and 21 additional existing systematic reviews and meta-analyses were assessed. The guidelines comprising 25 recommendations and one good practice statement (**Table I**) were published on November 15, 2022. Of the recommendations, 11 are new and 14 are updated and the

Table I WHO Recommendations for the Care of the Preterm or Low Birth Weight Infant

| <i>Recommendations</i> | <i>Status</i> | <i>Strength</i> |
|--|---------------|-----------------|
| <i>Preventive and Promotive Care</i> | | |
| <i>Any kangaroo mother care (KMC):</i> KMC is recommended as routine care for all preterm or low birth weight (LBW) infants. KMC can be initiated in the health-care facility or at home and should be given for 8-24 h per day. | Updated | Strong |
| <i>Immediate KMC:</i> KMC for preterm or LBW infants should be started as soon as possible after birth. | New | Strong |
| <i>Mother's own milk:</i> MOM is recommended for feeding of preterm or LBW infants, including very preterm (< 32 wk gestation) or very LBW (< 1.5 kg) infants. | Updated | Strong |
| <i>Donor human milk:</i> When MOM is not available, donor human milk may be considered for feeding of preterm or LBW infants, including very preterm or very LBW infants. | Updated | Conditional |
| <i>Multi-component fortification of human milk:</i> Multi-component fortification of human milk is not routinely recommended for all preterm or LBW infants but may be considered for very preterm or very LBW infants who are fed mother's own milk or donor human milk. | Updated | Conditional |
| <i>Preterm formula:</i> When mother's own milk and donor human milk are not available, nutrient-enriched preterm formula may be considered for very preterm or very LBW infants. | Updated | Conditional |
| <i>Early initiation of enteral feeding:</i> Preterm and LBW infants, including very preterm (< 32 wk gestation) and very LBW (< 1.5 kg) infants, should be fed as early as possible from the first day after birth. Infants who are able to breastfeed should be put to the breast as soon as possible after birth. Infants who are unable to breastfeed should be given expressed mother's own milk as soon as it becomes available. If mother's own milk is not available, donor human milk should be given wherever possible. | Updated | Strong |
| <i>Responsive and scheduled feeding:</i> In health-care facilities, scheduled feeding may be considered rather than responsive feeding for preterm infants born before 34 weeks' gestation, until the infant is discharged. | Updated | Conditional |
| <i>Fast and slow advancement of feeding:</i> In preterm or LBW infants, including very preterm (< 32 wk gestation) or very LBW (< 1.5 kg) infants, who need to be fed by an alternative feeding method to breastfeeding (e.g. gastric tube feeding or cup feeding), feed volumes can be increased by up to 30 mL/kg per day. | Updated | Conditional |
| <i>Duration of exclusive breastfeeding:</i> Preterm or LBW infants should be exclusively breastfed until 6 mo of age. | Updated | Strong |
| <i>Iron supplementation:</i> Enteral iron supplementation is recommended for human milk fed preterm or LBW infants who are not receiving iron from another source. | Updated | Strong |
| <i>Zinc supplementation:</i> Enteral zinc supplementation may be considered for human milk-fed preterm or LBW infants who are not receiving zinc from another source. | Updated | Conditional |
| <i>Vitamin D supplementation:</i> Enteral vitamin D supplementation may be considered for human milk-fed preterm or LBW infants who are not receiving vitamin D from another source. | Updated | Conditional |
| <i>Vitamin A supplementation:</i> Enteral vitamin A supplementation may be considered for human milk-fed | Updated | Conditional |

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Table I continued from pre-page

| Area of interest | Recommendations | Status | Strength |
|------------------|---|---------|-------------------------|
| | very preterm (< 32 weeks' gestation) or very LBW (< 1.5 kg) infants who are not receiving vitamin A from another source. | | |
| | <i>Probiotics</i> : May be considered for human-milk-fed very preterm infants (< 32 wk gestation). | New | Conditional |
| | <i>Emollients</i> : Application of topical oil to the body of preterm or LBW infants may be considered. | New | Conditional |
| | <i>Care of Complications</i> | | |
| | <i>CPAP for respiratory distress syndrome</i> : Continuous positive airway pressure (CPAP) therapy is recommended in preterm infants with clinical signs of respiratory distress syndrome. | Updated | Strong |
| | <i>CPAP immediately after birth</i> : CPAP therapy may be considered immediately after birth for very preterm infants, with or without respiratory distress. | New | Conditional |
| | <i>CPAP Pressure sources</i> : For preterm infants who need CPAP therapy, bubble CPAP may be considered rather than other pressure sources. | New | Conditional |
| | <i>Methylxanthines for treatment of apnea</i> : Caffeine is recommended for the treatment of apnea in preterm infants. | New | Strong |
| | <i>Methylxanthines for extubation</i> : Caffeine is recommended for the extubation of preterm infants born before 34 wk gestation. | New | Strong |
| | <i>Methylxanthines for prevention of apnea</i> : Caffeine may be considered for the prevention of apnea in preterm infants born before 34 wk gestation. | New | Conditional |
| | <i>Family Involvement and Support</i> | | |
| | <i>Family involvement</i> : Family involvement in the routine care of preterm or LBW infants in health-care facilities is recommended. | New | Strong |
| | <i>Family support</i> : Families of preterm or LBW infants should be given extra support to care for their infants, starting in healthcare facilities from birth and continued during follow-up post-discharge. The support may include education, counselling and discharge preparation from health workers, and peer support. | New | Conditional |
| | <i>Home visits</i> : Home visits by trained health workers are recommended to support families to care for their preterm or LBW infant. | New | Strong |
| | <i>Parental leave and entitlements</i> : Parental leave and entitlements should address the special needs of mothers, fathers and other primary caregivers of preterm or LBW infants. | New | Good practice statement |

good practice statement is a new addition. Some of the newer recommendations include the concept of Immediate KMC, the use of caffeine for the prevention of apnea and extubation, use of CPAP immediately after birth, emphasizing the importance of family involvement and home visits, the use of probiotics and emollients and the need for education and counselling, peer support and discharge preparedness. They were sub-categorized into three categories viz., preventive and promotive care (16 recommendations), care of complications (6 recommendations), and family involvement and support (3 recommendations)

A good practice statement was made for parental leave and entitlements, as although the evidence favoring this is limited but there is an obvious associated benefit.

THE WAY FORWARD

The panel also identified the knowledge gaps and listed the priority research questions that need further

evaluation, some of which are provided in **Box I**. The GDG also proposed implementation considerations for each recommendation and reflected on the principle of adopting, adapting, and implementing, to ensure quality care in accordance with a human rights-based approach. The members emphasized to focus strategically on a phased approach for facilitating the implementation and for overcoming the barriers. The implications demand innovative policies, the building of infrastructure, adequate manpower, apt finances and safe service delivery. The impact of these guidelines is planned to be monitored at the various health services including at national and subnational levels on clearly pre-defined criteria and indicators that are associated with locally agreed targets.

Integrating the new WHO guidelines to provide the best services in favor of small and sick neonates requires enthusiasm and commitment by the policymakers both in terms of financial help and for structured framework. This

Box I Some Suggested Research Areas in Preterm and Low Birthweight Care

- What is the effectiveness of KMC on longer-term (i.e., up to 2 years of age, school-age, adolescence) growth, neurodevelopment, behavior, mental health and disability outcomes?
- What is the effectiveness of immediate KMC in critically ill preterm or LBW infants?
- How can immediate KMC be scaled up in routine health systems?
- How can exclusive breastfeeding be promoted, supported and scaled up for preterm or LBW infants, especially those who are very preterm or very LBW?
- What are the most effective early feeding strategies for very preterm or very LBW infants, infants with illnesses (e.g. post-surgery), and infants with other conditions (e.g. doppler abnormalities, severe growth restriction)?
- What is the effectiveness, safety and feasibility of human milk banks in LMICs?
- What is the effectiveness and safety of probiotics in human-milk-fed infants?
- What is the effect of probiotics on immune function and gut microbiome in preterm or LBW infants?
- What are the most optimal probiotic compositions for preterm or LBW infants – that is, the optimal combination of genera, species and strains?
- What is the optimal probiotics regimen (dosage and duration) for preterm or LBW infants?
- What is the effectiveness of probiotics alone compared with a combination of probiotics and prebiotics for preterm or LBW infants?
- What is the role of probiotics in the prevention and management of postnatal growth restriction in preterm infants?
- What is the effect of emollients on mortality, invasive infection, sepsis, growth and longer-term neurodevelopment in preterm or LBW infants?
- What is the effect of emollients on thermoprotection and the microbiome in preterm or LBW infants?
- Which emollients (which oils, which composition) are most effective and safe for preterm or LBW infants?
- What is the optimal regime (dose, frequency, duration) and mode of application (e.g. non touch applications) for very or extremely preterm infants?
- What is the effectiveness of CPAP compared with humidified high-flow nasal cannula and other forms of non-invasive ventilation in preterm or LBW infants with respiratory distress syndrome?
- What strategies can be used to increase family participation in the care of their preterm or LBW infants in intensive and special care units, and in settings without dedicated newborn units?
- What is the most effective type of family support (including education, counselling, discharge preparation, peer support) for families of preterm or LBW infants?
- What is the effectiveness of standard in-person home visits compared with digital home visits (e.g. online video, mobile application [app], mHealth) for post-discharge follow-up of preterm or LBW infants?
- What is the feasibility of digital home visits in low-, middle- and high-income countries?

also demands the active participation of healthcare professionals who would serve as the frontline workers involved in the actual implementation of these policies to transform the recommendations into actions, so as to make the frame shift change in maternal and neonatal health.

Country level initiatives need to be taken for implementation of the various evidence-based guidelines for ensuring quality care of preterm and LBW infants at facility and community level. There is scope for adopting these *in toto*, or adapting some or all based on country needs and equity considerations.

India as a country has been the torch bearer for facility based newborn care (Special care newborn units, Newborn stabilization units and Newborn care corners) and the country's experiential learning has paved way for development of global framework for care of small & sick newborn. We are well poised to adopt all the components

of these guidelines in the clinical care of our neonates both in the public and private sector. Challenges anticipated in ensuring uniformity in implementation should be predicted and addressed at the inception to reap full benefits. Research areas spelled out for different domains should be explored both at the individual clinical and at systems level.

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