Nutritional Management of the Low Birth Weight/Preterm Infant in Community Settings: A Perspective from the Developing World

Aamer Imdad, MBBS and Zulfiqar A. Bhutta, MBBS, FRCP, FRCPCH, FCPS, PhD

Globally, about 20 million infants are born with low birth weight (LBW; <2500 g). Of all LBW infants, approximately 95% are born in developing countries. The greatest incidence of LBW occurs in South-Central Asia; the second greatest is in Africa. The two main reasons for LBW are preterm birth (<37 weeks) and intrauterine growth restriction (IUGR), which are risk factors for increased morbidity and mortality in newborn infants. Maternal nutrition status is one of the most important risk factors for LBW/IUGR. Providing balanced protein energy and multiple micronutrient supplements to pregnant women will reduce incidence of IUGR. Calcium supplementation during pregnancy will reduce the incidence of pre-eclampsia and preterm birth in developing countries. Exclusive breastfeeding is protective for a mother and her infant and has been shown to reduce morbidity and mortality in infancy. Kangaroo mother care for preterm infants will reduce severe morbidity and mortality as well. Community-based intervention packages are among the most effective methods of reducing morbidity and mortality in mothers and children. Future research should focus on improving triage of preterm and IUGR infants. Exclusive breastfeeding should be promoted, and appropriate alternative food supplements should be provided when breastfeeding is not possible. *(J Pediatr 2013;162:S107-14)*.

During the past decade, child mortality before the age of 5 years has decreased markedly. The child death rate was 10.6 million/year in 2000-2003; it decreased to 8.8 million in 2008.[1,2] A reduction in mortality among children 1 to 59 months of age accounts for most of this decline. This may be because child-survival programs have focused primarily on important causes of death after the first 4 weeks of life (ie, pneumonia, diarrhea, malaria, and vaccine-preventable disorders).[3] At the same time, little progress has been made in reducing neonatal mortality.[4] Neonatal deaths now account for 41% of deaths compared with 37% from 2000 to 2003.[1,2] To achieve the Millennium Development Goal 4 to reduce child mortality by two-thirds by 2015, it is important to reduce neonatal deaths.[3]

Low birth weight (LBW) increases morbidity and mortality in neonates and is a common feature in most neonatal deaths.[3,5,6] LBW may result from preterm birth, intrauterine growth restriction (IUGR), or both.[7] Preterm infants are 7 to 13 times more likely to die during the neonatal period than full-term infants.[8-10] Infants who are preterm with IUGR have an even greater risk of death.[11] A term LBW infant is likely to have growth failure and an increased risk of morbidity and mortality in infancy.[12] It has been estimated that the risk for neonatal death is 2.8 or 8 times greater for term infants who weigh 1500 to 1999 g at birth than for infants who weigh 2000 to 2499 g or 2500 to 2999 g, respectively.[13] LBW infants who survive are likely to remain small and more likely to experience developmental deficits than normal-term infants.[14] Adults who had LBWs have a greater incidence of chronic diseases such as type 2 diabetes, hypertension, and other cardiovascular disease.[14,15]

According to the United Nations Children's Fund (UNICEF), an estimated 15.5% (>20 million infants) of all births were LBW (<2500 g) worldwide in the year 2000.[5] The prevalence of LBW infants in developing countries (16.5%) is more than double than in developed countries (7%). The vast majority (95%) of LBW infants are born in developing countries, with the greatest incidence in South-Central Asia (27%) followed by Africa, where incidence ranges from 13% to 15%, with little variation across the region as a whole. Overall, ~70% all LBW births occur in Asia.[5]

The causes of LBW are different in developing and developed countries.[16] Preterm birth is major cause of LBW in developed countries, whereas most LBW newborns are born at term but small for gestational age (SGA) in developing nations.[17] SGA infants are defined as infants whose weight is below the 10th percentile or 2 SD below the mean in growth charts for their estimated gestational age.[18] Accurate assessment of gestational age is required to screen SGA infants. Because it is relatively difficult to get accurate gestational age estimates, birth weight is the most commonly used variable used to compare different populations.[16] Infants born with LBW at term have IUGR, whereas the subcategory very LBW comprises mainly preterm

BMI	Body mass index
IUGR	Intrauterine growth restriction
LBW	Low birth weight
$MgSO_4$	Magnesium sulfate
RR	Relative risk
SGA	Small for gestational age
UNICEF	United Nations Children's Fund

From the Division of Women & Child Health, The Aga Khan University, Karachi, Pakistan

Please see the Author Disclosures at the end of this article.

 http://dx.doi.org/10.1016/j.jpeds.2012.11.060

infants. Indeed, these 2 categories overlap because some preterm infants exhibit features of IUGR and other newborn infants with evidence of IUGR may weigh more than 2500 g at birth, and, thus, are not considered LBW.[16] In developing countries, it is difficult to assess and evaluate LBW infants and monitor rates of neonatal mortality because data are incomplete. It is estimated that 58% of newborn infants are not even weighed at birth in developing countries.[5] The incidence is greatest in south Asia and sub-Saharan Africa, where 74% and 65% of births are not weighed, respectively.[5]

We reviewed the evidence base for strategies designed to manage LBW/preterm infants in community settings in the developing world to make specific recommendations for action. We searched PubMed, Cochrane Library, World Health Organization/UNICEF data bases and guidelines by using a combination of terms for "low birth weight," "community," "nutrition," etc, and synthesized up-to-date evidence on nutritional management of LBW infants in the community.

Etiology of LBW

The causes of fetal growth restriction and prematurity in developing countries are well known.[16,19] Some of the most important maternal risk factors include: low prepregnancy weight or body mass index (BMI); inadequate energy intake and gestational weight gain; cigarette smoking; and specific complications of pregnancy, such as genital tract infections, pregnancy-induced hypertension, and incompetent cervix.[3,16,19] Fetuses with certain genetic or chromosomal disorders are also at greater risk for IUGR.[20] The **Table** summarizes the main known risk factors in the pathogenesis of LBW/IUGR.[16,19] **Figure 1** describes the interaction of social, economic, and behavioral factors that can result in LBW/IUGR.[16]

The nutritional status of a woman before and during pregnancy is important for a healthy pregnancy outcome. Pregnancy is just one stage of a woman's life, and women living in a developing country become pregnant in a context of gender inequality, inadequate educational opportunities, malnutrition, marriage and conception at a young age, short birth intervals, and undesirably large families. **Figure 2** helps us to understand the cycle of malnutrition that runs among LBW, childhood/adolescent stunting, and maternal undernutrition and how repeated pregnancies with inadequate recovery between pregnancies can lead to maternal depletion syndrome.[21]

Maternal undernutrition is widespread in low and middle-income countries, especially in South-Central Asia where more than 10% of women 15 to 49 years old are <145 cm tall and show evidence of maternal wasting (BMI <18.5) in most countries.[13] A serious problem of maternal undernutrition (more than 20% of women with BMI <18.5) is evident in most countries in sub-Saharan Africa, South-Central/South-Eastern Asia. Yemen, India, Bangladesh, and Eritrea have a critical problem because BMI is low in about 40% of all women.[13]

Low prepregnancy weight and BMI are important risk factors for LBW.[13,22] A recent meta-analysis of 78 studies that included 1 025 794 women has shown that maternal underweight is associated with an overall increased risk of preterm birth by 29% (relative risk [RR] 1.29; 95% CI 1.15-1.46) and that of LBW by 64% (RR 1.64; 95% CI 1.38-1.94).[23] A subgroup analysis showed that underweight women have an increased risk of preterm birth in developing countries (RR 1.22; 95% CI 1.15-1.30) but not in developed countries (RR 0.99; 95% CI 0.67-1.45). In both developed and developing countries, underweight women are at increased risk of LBW births (RR 1.48; 95% CI 1.29-1.68 and RR 1.52; 95% CI 1.25-1.85, respectively).

In addition to maternal nutrition status, increased physical activity performed by women, such as farming or gathering water, is reported to be associated with lower birth weights and smaller head and mid-arm circumferences in infants.[24] Malaria during pregnancy is associated with LBW,[16] and malaria chemoprophylaxis increases maternal hemoglobin levels and infant birth weights.[25] In addition, women in

Table. Selected risk factors for LBW

Prepregnancy	Pregnancy	Social and environmental
Low weight for height	Multiple gestation	Low socioeconomic status
Short stature	Birth order	Low educational status
Chronic medical illness	Anemia	Smoking
Poor nutrition	Elevated hemoglobin	No care or inadequate prenatal care
Low maternal weight at mother's birth	concentration	Poor gestational weight gain
Previous infant of LBW	Fetal disease	Alcohol abuse
Uterine or cervical anomalies	Pre-eclampsia and hypertension	Illicit and prescription drugs
Parity (none or more than 5)	Infections	Short interpregnancy intervals (<6 months)
	Placental problems	Age (<16 or >35 years)
	Premature rupture of membranes	Unmarried
	Heavy physical work	Stress (physical and psychological)
	Altitude	
	Renal disease	
	Assisted reproductive technology	
	Exposure to indoor air pollution	
	Maternal psycho-social stress	
	Mental health	

Data derived from Qadir and Bhutta[16] and Valero De Bernabe et al.[19]

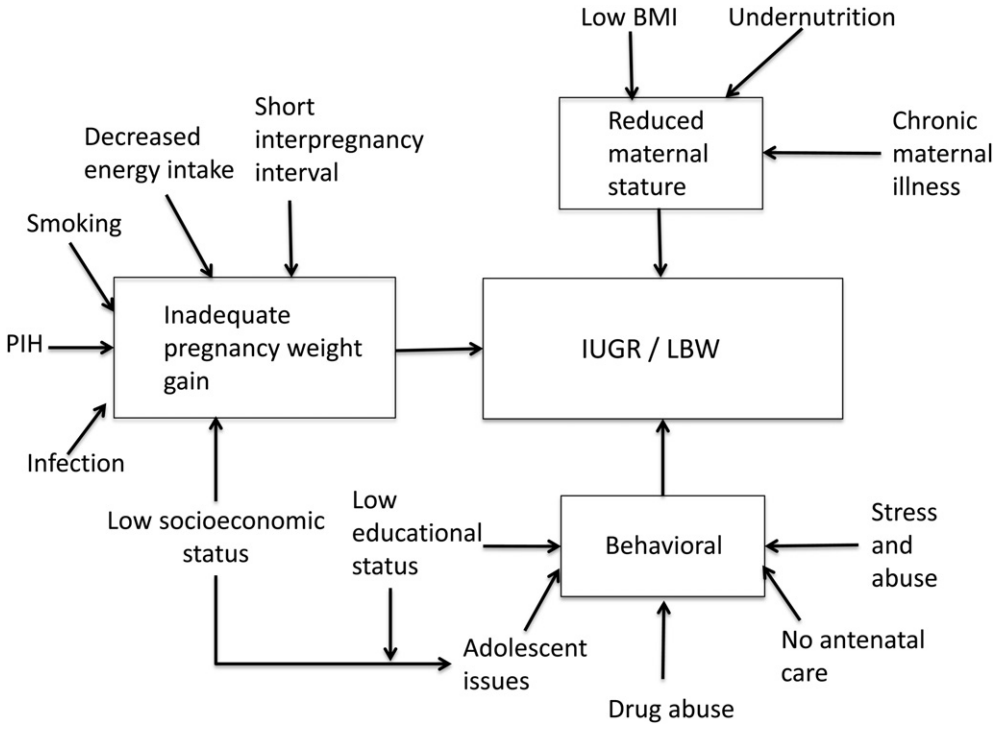

Figure 1. Factors associated with LBW. *PIH*, pregnancy induced hypertension. Figure used with permission from Qadir A et al.[16]

developing countries may suffer from chronic and communicable diseases, which further aggravate their already poor nutritional status. Certain social factors like drug abuse, poor nutritional habits, and cigarette smoking are interrelated and covary with poor socioeconomic status.[16] Some of the other key risk factors associated with LBW are indoor air pollution, environmental tobacco smoke, and maternal mental health.[16,25,26]

Interventions to Prevent LBW

Prevention and management of LBW in the community requires a continuum of care and coordination among reproductive health services that provide family planning support, such as antenatal care for pregnant women, skilled attendance and emergency obstetric care during birth, and postnatal care services.[6,16] **Figure 3** summarizes evidence-based interventions that can help prevent and manage morbidity and mortality in LBW infants. We focus on nutrition interventions that can help to prevent or manage the LBW and/or preterm infant in the community.

Birth Spacing

The relationship of adequate birth spacing (>36 months) and neonatal and infant outcomes is well known.[27-30] Short birth intervals increase the risk of LBW, preterm birth, neonatal mortality, and stunting.[27,31-33] A meta-analysis by Conde-Agudelo et al[32] has shown that inter-pregnancy intervals shorter than 6 months are associated with an increased risk of preterm birth compared with interpregnancy intervals of 18-23 months (OR 1.40; 95% CI 1.24-1.58), LBW (OR 1.61; 95% CI 1.39-1.86), and SGA (OR 1.26; 95% CI 1.18-1.33). A retrospective study of 45 000 women has shown that the women who use family planning services are less likely to deliver a LBW infant than those who do not.[34]

Maternal Nutrition Interventions

Low folate levels are associated with LBW, preterm birth, and IUGR.[35-39] Folic acid supplementation around the time of conception reduces the incidence of neural tube defects and other congenital anomalies.[40,41] Folate supplementation reduces the incidence of preterm birth and LBW.[35,42,43] Most of this evidence is based on observational and nonrandomized studies; any recommendation for providing folate supplements to preterm and/or LBW infants should be made after the intervention has been tested in randomized trials.

Balanced protein energy supplementation is considered one of the most promising macronutrient interventions for the prevention of adverse perinatal outcomes, including IUGR.[44,45] A recent meta-analysis of randomized studies indicate that balanced protein energy supplementation in pregnancy is associated with a 31% reduction in the risk of giving birth to an SGA infant (RR 0.69; 95% CI 0.56-0.85).[46] It also increases mean birth weight (mean difference, +59 g; 95% CI 33-86). This effect is more pronounced in malnourished women than adequately nourished women. The authors of a Cochrane review of balanced protein energy supplementation has also concluded that risk of stillbirth was significantly reduced for women given balanced energy and protein

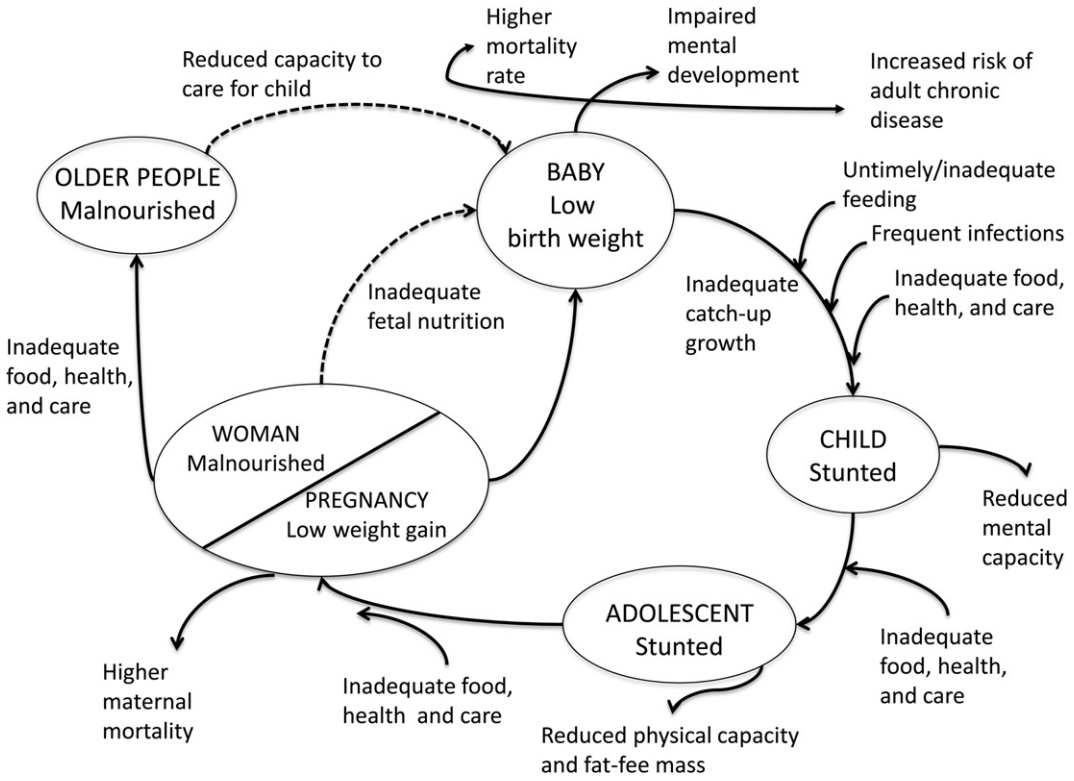

Figure 2. Nutrition across the life cycle. Figure created by United Nations Administrative Committee on Coordination, Sub-Committee on Nutrition and reproduced per United Nations Administrative Committee on Coordination, Sub-Committee on Nutrition policy.[21]

supplementation (RR 0.62, 95% CI 0.40-0.98), mean birth weight was significantly increased (mean difference +40.96 g; 95% CI 4.66-77.26).[45] There also was a significant reduction in the risk of SGA (RR 0.79, 95% CI 0.69-0.90). No significant effect was detected for preterm birth or neonatal death.[45]

Micronutrient deficiency is common in most low- and middle-income countries.[13,47,48] Iron deficiency is one of the leading micronutrient deficiencies among pregnant women in these countries.[49] For example, anemia affects 41.8% of all pregnancies globally,[50] and iron deficiency accounts for half of these cases.[51] Intermittent or daily iron or iron-folic acid supplementation during pregnancy increases hemoglobin levels and decreases the incidence of anemia at term.[52]

Because maternal micronutrient deficiencies during pregnancy in developing countries are common, there is interest in administering multiple micronutrients during pregnancy as an alternative to traditional iron-folic acid combinations.[53] UNICEF has developed such a formulation called the United Nations Multiple Micronutrient Preparation in close collaboration with the United Nations University and the World Health Organization.[48] The authors of a Cochrane review showed that multiple micronutrient supplementation has comparable effects on maternal anemia in the third trimester (RR 1.03; 95% CI 0.87-1.22) and reduces the risk of SGA births by 9% (RR 0.91; 95% CI 0.86-0.96) compared with iron-folate supplementation.[54] A meta-analysis of 12 randomized, controlled trials has shown that multiple micronutrient supplementation is associated with an increase in mean birth weight (mean difference, 22.4 g; 95% CI 8.3-36.4 g); a reduction in the prevalence of LBW (OR 0.89; 95% CI 0.81-0.97) and SGA (OR 0.90; 95% CI 0.82-0.99); and an increase in the prevalence of large-for-gestational-age babies (OR 1.13; 95% CI 1.00-1.28).[53] Another recent meta-analysis that included 17 trials has shown that multiple micronutrient supplements reduces incidence of SGA by 9% (RR 0.91; 95% CI 0.86-0.96 [fixed model]).[55]

Recently, there has been an increased interest in providing combined macro/micronutrient supplements because deficiencies for both exist concurrently. A study from Burkina Faso has shown that supplementation with balanced protein energy and multiple micronutrients increases length at birth more than supplementation with multiple micronutrients alone.[56] Future research efforts should focus on validating these results in other parts of the world.

Calcium and Magnesium Supplementation during Pregnancy

Hypertensive disorders of pregnancy increase maternal morbidity and mortality and are associated with preterm birth and IUGR.[57,58] Women with pre-eclampsia are 2.7 times more likely than normotensive women to have infants with

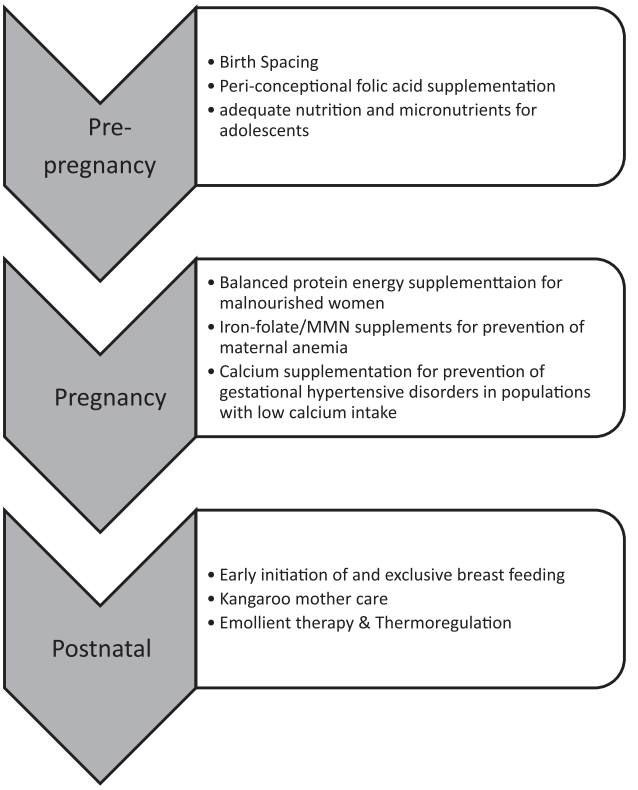

Figure 3. Proposed nutrition related interventions for prevention and management of LBW/preterm birth in community settings. *MMN*, maternal multiple micronutrient.

IUGR.[57] Calcium supplementation during pregnancy reduces gestational hypertensive disorders and risk of preterm birth. A Cochrane review by Hofmeyr et al[59] has shown that calcium supplementation during pregnancy significantly reduces the incidence of gestational hypertension (RR 0.65; 95 % CI 0.53-0.81), preeclampsia (RR 0.45; 95% CI 0.31-0.65), and preterm birth (RR 0.76; 95% CI 0.60-0.97). Another recent review of studies from developing countries shows similar results for reduction in risk of gestational hypertension (RR 0.55; 95% CI 0.36-0.85), pre-eclampsia (RR 0.41; 95% CI 0.24-0.69), and preterm birth (RR 0.88; 95% CI 0.78-0.99).[60] Magnesium sulfate ($MgSO_4$) supplementation effectively prevents eclampsia in women with pre-eclampsia.[51] A Cochrane review that included 6 trials for $MgSO_4$ analysis shows that $MgSO_4$ supplementation reduces the risk of eclampsia (RR 0.41; 95% CI 0.29-0.58) and placental abruption (RR 0.64; 95% CI 0.50-0.83) in pre-eclamptic women.[61]

Breastfeeding

Breast milk is the natural and ideal first food for infants, including those born with LBW; it provides many immunologic, psychological, and social, economic, and environmental benefits.[62-64] Breastfeeding should be initiated within 24-48 hours after birth and continued as the sole source of nutrition for the first 6 months of life.[65] Suboptimal breastfeeding is a risk factor for increased morbidity and mortality in infants.[66] Partially breastfed infants have 3 times the risk of all-cause mortality, and those who do not breastfeed have 14 times the risk of death in the first 6 months of life compared with those who breastfeed exclusively.[13] A study from Ghana has shown that the risk of neonatal death is 4-fold greater in children given milk-based fluids or solids in addition to breast milk.[67] There is increasing risk of neonatal mortality with increasing delay in initiation of breastfeeding from 1 hour to day 7. Late initiation of breastfeeding (after day 1) is associated with a 2.4-fold increase in risk of mortality. Another study from Bangladesh has shown that partial or no breastfeeding is associated with a 2.23-fold greater risk of infant deaths resulting from all causes and 2.40- and 3.94-fold greater risk of deaths attributable to acute respiratory infections and diarrhea, respectively, compared with exclusive breastfeeding in the first few months of life.[68]

Exclusive breastfeeding is not common in most countries.[69,70] Exclusive breastfeeding rates vary from 20% in central and eastern European countries to 44% in South Asia.[71] Exclusive breastfeeding for 6 months might be difficult, particularly where maternal malnutrition is common.[72] One of the main contributing factors is the lack of assistance to mothers who wish to breastfeed.[73] Education and support is, therefore, the cornerstone for the promotion of breastfeeding.[74] The Baby Friendly Hospital Initiative and peer counselors are considered the two most effective strategies to promote exclusive breastfeeding, especially when infants are delivered at home.[65]

Comprehensive and culturally appropriate breastfeeding education provided by counselors (physicians, nurses, midwives, lactation consultants, or peer counselors) in the hospital during the prenatal period and continued support in the mother's home is critical for facilitating breastfeeding among mothers, especially those who have low incomes.[75-77] Prenatal and postnatal education is important because the incidence of breastfeeding is affected primarily by prenatal education, whereas prenatal and postpartum management affects the duration and exclusivity of breastfeeding.[78,79]

The authors of a Cochrane review have evaluated support for the breastfeeding mother and show that all forms of extra support increases the duration of "any breastfeeding" (RR 0.91; 95% CI 0.86-0.96) and increases likelihood of exclusive breastfeeding compared with any breastfeeding (RR 0.81; 95 % CI 0.74-0.89).[80] A review published in *the Lancet* Undernutrition series shows that individual counseling increases the odds of exclusive breastfeeding substantially during the neonatal period (OR 3.45; 95% CI 2.20-5.42) and at 6 months after delivery (OR 1.93; 95% CI, 1.18-3.15).[65] Group counseling is also effective during the neonatal period (OR 3.88; 95% CI 2.09-7.22) and at 6 months after delivery (OR 5.19; 95% CI 1.90-14.15). Mass media campaigns have been shown to increase rates of exclusive breastfeeding.

Kangaroo Mother Care

Kangaroo mother care is a simple and cost-effective method to promote the health and well-being of preterm infants.[81] It

is an effective way to meet an infant's needs for warmth, breastfeeding, protection from infection, stimulation, safety, and love. Its key features include early, continuous and prolonged skin-to-skin contact between the mother and the infant, exclusive breastfeeding, and support provided during the hospital stay and continued at home.

Kangaroo mother care has been shown to reduce morbidity and mortality in preterm infants. A recent review for the Lives Saved Tool by Lawn et al[82] has shown that kangaroo mother care in the first week of life reduced neonatal mortality by 51% (RR 0.49; 95% CI 0.29-0.82) compared with standard care. A meta-analysis of 5 randomized controlled trials suggested significant reductions in serious morbidity for infants <2000 g (RR 0.34; 95% CI 0.17-0.65).[82] Kangaroo mother care can be practiced in facility as well as community settings. These benefits may also be evident in facilities in developing countries. Mother-infant dyads that practice kangaroo mother care have reduced rates of mortality and lengths of stay.[83]

Skin Barrier Therapy for Preterm Infants

An important determinant of the high morbidity and mortality rates for preterm infants is the integrity of the skin barrier.[84] The immature skin barrier allows high rates of transepidermal water loss and concomitant loss of fluid and heat and increases the susceptibility to invasive infections.[85-87] Enhancement of the skin barrier through topical emollient therapy reduces morbidity and mortality in preterm infants.[88-90] A randomized trial from Bangladesh has shown that applying sunflower oil to the skin of preterm infants reduces sepsis by 41% and mortality by 26%.[88]

On the other hand, a multicenter study of extremely LBW preterm infants (birth weight <1000 g) indicates that application of a commercially available emollient ointment has no effect on neonatal mortality.[90] Although the evidence is not conclusive, a Cochrane review has shown that emollient interventions improves daily weight gain by 5.1 g (95% CI 3.5-6.7), reduces length of stay by 4.5 days (95% CI 2.4-6.5) and has a slight, positive effect on postnatal complications and weight gain at 4-6 months.[91] Another noteworthy intervention for preterm infants is swaddling; infants who are swaddled have improved neuromuscular development, less physiologic distress, better motor organization, and more self-regulatory ability than those who are not.[92]

Discussion

Despite a number of limitations and gaps in evidence, there is sufficient knowledge to recommend strategies to prevent and mitigate morbidity and mortality of the LBW and/or preterm infant in the developing world. Addressing maternal undernutrition and risk factors for IUGR through evidence-based interventions such as balanced energy protein supplements and strategies to address food insecurity can be fruitful. In addition, addressing maternal micronutrient deficiencies and reducing the burden of morbidity and malaria are important. In the long term, reducing family size and increasing interpregnancy intervals may also reduce maternal depletion and improve birth weight.

On the basis of current evidence and the context of nutritional management and thermal care of these infants, early and exclusive breastfeeding is of key importance. Strategies to address maternal antenatal care and promotion of breastfeeding include providing education and support through community support groups and trained health workers. Outreach services provided by lay health workers and community structures offer the best platform for promoting context-specific packages of early newborn care and for reaching those in greatest need.

There is overwhelming evidence to support breastfeeding or breast milk feeding of LBW and preterm infants in developing countries. It is now recommended that mothers with HIV should breastfeed their infants when the infant or mother is on effective antiretroviral therapy.

It is also important to underscore the need for further studies in these areas where there is limited evidence. The criteria used to identify and triage preterm (early and late) and SGA infants at birth should be made cost-effective and available to communities with minimal resources (eg, robust and economical weighing scales should be made more widely available). When breastfeeding is not possible, products that are nutritionally adequate for preterm infants (<35 weeks' gestation or <1500 g birth weight) should be made available. The provision and promotion of these nutritional alternatives should be done in a way that does not impact current breastfeeding strategies and recommendations. Supplements developed for breastfed preterm infants should be designed with due consideration of the protein/energy and micronutrient needs, safety studies, and risk-benefit analyses that are appropriate for the developing world. Improved reference standards for intrauterine and postnatal growth for infants that define "optimal" growth should consider the global population of preterm infants. ■

Author Disclosures

Both authors received an honorarium from Mead Johnson Nutrition for attendance, presentation, and manuscript preparation. Both authors contributed the first draft of this manuscript.

Reprint requests: Zulfiqar A. Bhutta, MBBS, FRCP, FRCPCH, FCPS, PhD, Noordin Noormahomed Sharief Endowed Professor & Founding Chair, Division of Women & Child Health, The Aga Khan University, Karachi 74800, Pakistan. E-mail: zulfiqar.bhutta@aku.edu.

References

1. Bryce J, Boschi-Pinto C, Shibuya K, Black RE. WHO estimates of the causes of death in children. Lancet 2005;365:1147-52.
2. Black RE, Cousens S, Johnson HL, Lawn JE, Rudan I, Bassani DG, et al. Global, regional, and national causes of child mortality in 2008: a systematic analysis. Lancet 2010;375:1969-87.
3. Lawn JE, Kerber K, Enweronu-Laryea C, Cousens S. 3.6 million neonatal deaths—what is progressing and what is not? Semin Perinatol 2010;34:371-86.

4. You D, Wardlaw T, Salama P, Jones G. Levels and trends in under-5 mortality, 1990-2008. Lancet 2010;375:100-3.
5. World Health Organization and United Nations Children's Fund. Low birthweight. Country, regional, and global estimates. Geneva and New York: WHO/UNICEF; 2004. p. 1-32.
6. Lawn JE, Kerber K, Enweronu-Laryea C, Massee Bateman O. Newborn survival in low resource settings—are we delivering? BJOG 2009; 116(suppl 1):49-59.
7. Sachdev HP. Low birth weight in South Asia. Int J Diab Dev Ctries 2001; 21:13-33.
8. Gouyon JB, Vintejoux A, Sagot P, Burguet A, Quantin C, Ferdynus C. Neonatal outcome associated with singleton birth at 34-41 weeks of gestation. Int J Epidemiol 2010;39:769-76.
9. Khashu M, Narayanan M, Bhargava S, Osiovich H. Perinatal outcomes associated with preterm birth at 33 to 36 weeks' gestation: a population-based cohort study. Pediatrics 2009;123:109-13.
10. Yasmin S, Osrin D, Paul E, Costello A. Neonatal mortality of low-birthweight infants in Bangladesh. Bull World Health Organ 2001;79:608-14.
11. Lawn JE, Gravett MG, Nunes TM, Rubens CE, Stanton C. Global report on preterm birth and stillbirth (1 of 7): definitions, description of the burden and opportunities to improve data. BMC Pregnancy Childbirth 2010;10(suppl 1):S1.
12. Ashworth A. Effects of intrauterine growth retardation on mortality and morbidity in infants and young children. Eur J Clin Nutr 1998;52(suppl 1):S34-41.
13.. Black RE, Allen LH, Bhutta ZA, Caulfield LE, de Onis M, Ezzati M, et al. Maternal and child undernutrition: global and regional exposures and health consequences. Lancet 2008;371:243-60.
14. Martorell R, Ramakrishnan U, Schroeder DG, Melgar P, Neufeld L. Intrauterine growth retardation, body size, body composition and physical performance in adolescence. Eur J Clin Nutr 1998;52(suppl 1):S43-52.
15. Ferro-Luzzi A, Ashworth A, Martorell R, Scrimshaw N. Report of the IDECG Working Group on effects of IUGR on infants, children and adolescents: immunocompetence, mortality, morbidity, body size, body composition, and physical performance. Eur J Clin Nutr 1998;52(suppl 1):S97-9.
16. Qadir A, Bhutta ZA. Low birthweight in developing countries. In: Kiess W, Chernausek SD, Hokken-Koelega ACS, eds. Small for gestational age causes and consequences. Basel: Karger; 2009. p. 148-62.
17. Goplan C. LBWs: significance and implications. In: Sachdev HPS, Choudhury P, eds. Nutrition in children: developing country concerns. New Delhi: Department of Pediatrics, Maulana Azad Medical College; 1995. p. 1-33.
18. Bakketeig LS, Butte N, de Onis M, Kramer M, O'Donnell A, Prada JA, et al. Report of the IDECG Working Group on definitions, classifications, causes, mechanisms and prevention of IUGR. Eur J Clin Nutr 1998;52(suppl 1):S94-6.
19.. Valero De Bernabe J, Soriano T, Albaladejo R, Juarranz M, Calle ME, Martinez D, et al. Risk factors for low birth weight: a review. Eur J Obstet Gynecol Reprod Biol 2004;116:3-15.
20. Ashdown-Lambert JR. A review of low birth weight: predictors, precursors and morbidity outcomes. J R Soc Promot Health 2005;125:76-83.
21. United Nations Administrative Committee on Coordination, Sub-Committee on Nutrition (ACC/SCN). Fourth report on the world nutrition situation. Geneva: ACC/SCN in collaboration with IFPRI: United Nations ACC/SCN in collaboration with International Food Policy Research Institute (IFPRI); 2000. p. 1-140.
22. Abu-Saad K, Fraser D. Maternal nutrition and birth outcomes. Epidemiol Rev 2010;32:5-25.
23.. Han Z, Mulla S, Beyene J, Liao G, McDonald SD. Maternal underweight and the risk of preterm birth and low birth weight: a systematic review and meta-analyses. Int J Epidemiol 2011;40:65-101.
24.. Shaw GM. Strenuous work, nutrition and adverse pregnancy outcomes: a brief review. J Nutr 2003;133:1718S-21S.
25. Gulmezoglu M, de Onis M, Villar J. Effectiveness of interventions to prevent or treat impaired fetal growth. Obstet Gynecol Surv 1997;52:139-49.
26. Pope DP, Mishra V, Thompson L, Siddiqui AR, Rehfuess EA, Weber M, et al. Risk of low birth weight and stillbirth associated with indoor air pollution from solid fuel use in developing countries. Epidemiol Rev 2010;32:70-81.
27. Rutstein SO. Effects of preceding birth intervals on neonatal, infant and under-five years mortality and nutritional status in developing countries: evidence from the demographic and health surveys. Int J Gynaecol Obstet 2005;89(suppl 1):S7-24.
28. Akter S, Rahman JA, Rahman MM, Abedin S. The influence of birth spacing on child survival in bangladesh: a life table approach. World Health Popul 2010;12:42-56.
29. Zilberman B. Influence of short interpregnancy interval on pregnancy outcomes [in Hebrew]. Harefuah 2007;146:42-7. 78.
30. King JC. The risk of maternal nutritional depletion and poor outcomes increases in early or closely spaced pregnancies. J Nutr 2003;133:1732S-6S.
31. Dewey KG, Cohen RJ. Does birth spacing affect maternal or child nutritional status? A systematic literature review. Matern Child Nutr 2007;3: 151-73.
32. Conde-Agudelo A, Rosas-Bermudez A, Kafury-Goeta AC. Birth spacing and risk of adverse perinatal outcomes: a meta-analysis. JAMA 2006;295: 1809-23.
33. Zhu BP, Rolfs RT, Nangle BE, Horan JM. Effect of the interval between pregnancies on perinatal outcomes. N Engl J Med 1999;340:589-94.
34. Jamieson DJ, Buescher PA. The effect of family planning participation on prenatal care use and low birth weight. Fam Plann Perspect 1992; 24:214-8.
35. Takimoto H, Mito N, Umegaki K, Ishiwaki A, Kusama K, Abe S, et al. Relationship between dietary folate intakes, maternal plasma total homocysteine and B-vitamins during pregnancy and fetal growth in Japan. Eur J Nutr 2007;46:300-6.
36. Vollset SE, Refsum H, Irgens LM, Emblem BM, Tverdal A, Gjessing HK, et al. Plasma total homocysteine, pregnancy complications, and adverse pregnancy outcomes: the Hordaland Homocysteine study. Am J Clin Nutr 2000;71:962-8.
37. Scholl TO, Hediger ML, Schall JI, Khoo CS, Fischer RL. Dietary and serum folate: their influence on the outcome of pregnancy. Am J Clin Nutr 1996;63:520-5.
38. Lindblad B, Zaman S, Malik A, Martin H, Ekstrom AM, Amu S, et al. Folate, vitamin B12, and homocysteine levels in South Asian women with growth-retarded fetuses. Acta Obstet Gynecol Scand 2005;84: 1055-61.
39. van Eijsden M, Smits LJ, van der Wal MF, Bonsel GJ. Association between short interpregnancy intervals and term birth weight: the role of folate depletion. Am J Clin Nutr 2008;88:147-53.
40. Lumley J, Watson L, Watson M, Bower C. Periconceptional supplementation with folate and/or multivitamins for preventing neural tube defects. Cochrane Database of Systematic Reviews 2011;(Issue 4). Art. No.: CD001056, http://dx.doi.org/10.1002/14651858.CD001056.pub2.
41. Blencowe H, Cousens S, Modell B, Lawn J. Folic acid to reduce neonatal mortality from neural tube disorders. Int J Epidemiol 2010;39(suppl 1): i110-21.
42. Scholl TO, Hediger ML, Bendich A, Schall JI, Smith WK, Krueger PM. Use of multivitamin/mineral prenatal supplements: influence on the outcome of pregnancy. Am J Epidemiol 1997;146:134-41.
43. Rondo PH, Tomkins AM. Folate and intrauterine growth retardation. Ann Trop Paediatr 2000;20:253-8.
44. de Onis M, Villar J, Gulmezoglu M. Nutritional interventions to prevent intrauterine growth retardation: evidence from randomized controlled trials. Eur J Clin Nutr 1998;52(suppl 1):S83-93.
45. Ota E, Tobe-Gai R, Mori R, Farrar D. Antenatal dietary advice and supplementation to increase energy and protein intake. Cochrane Database Syst Rev 2012;9:CD000032.
46. Imdad A, Yakoob MY, Bhutta ZA. Effect of balanced protein energy supplementation during pregnancy on birth outcomes. BMC Public Health 2011;13(suppl 3):S17.
47. Black RE. Micronutrients in pregnancy. Br J Nutr 2001;85(suppl 2): S193-7.
48. Yakoob MY, Khan YP, Bhutta ZA. Maternal mineral and vitamin supplementation in pregnancy. Expert Rev Obstet Gynecol 2010;5:241-56.

49. Rusia U, Madan N, Agarwal N, Sikka M, Sood SK. Effect of maternal iron deficiency anaemia on foetal outcome. Indian J Pathol Microbiol 1995; 38:273-9.
50. World Health Organization (WHO). Worldwide prevalence of anaemia 1993-2005. WHO Global Database on Anaemia. In: de Benoist B, McLean E, Egli I, Cogswell M, eds. Geneva: WHO and Centers for Disease Contraol and Prevention (CDC) Atlanta; 2008. p. 1-51.
51. Bhutta ZA, Ali S, Cousens S, Ali TM, Haider BA, Rizvi A, et al. Alma-Ata: Rebirth and Revision 6 Interventions to address maternal, newborn, and child survival: what difference can integrated primary health care strategies make? Lancet 2008;372:972-89.
52. Peña-Rosas JP, Viteri FE. Effects and safety of preventive oral iron or iron+folic acid supplementation for women during pregnancy. Cochrane Database Syst Rev 2009 Oct 7;CD004736.
53. Fall CH, Fisher DJ, Osmond C, Margetts BM. Multiple micronutrient supplementation during pregnancy in low-income countries: a meta-analysis of effects on birth size and length of gestation. Food Nutr Bull 2009;30:S533-46.
54. Haider BA, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. Cochrane Database Syst Rev 2012 Nov 14. CD004905.
55. Batool AH, Yakoob MY, Bhutta ZA. Effect of multiple micronutrient supplementation during pregnancy on maternal and birth outcomes. BMC Public Health 2011;11(suppl 3):S19.
56. Huybregts L, Roberfroid D, Lanou H, Menten J, Meda N, Van Camp J, et al. Prenatal food supplementation fortified with multiple micronutrients increases birth length: a randomized controlled trial in rural Burkina Faso. Am J Clin Nutr 2009;90:1593-600.
57. Srinivas SK, Edlow AG, Neff PM, Sammel MD, Andrela CM, Elovitz MA. Rethinking IUGR in preeclampsia: dependent or independent of maternal hypertension? J Perinatol 2009;29:680-4.
58. Duley L. The global impact of pre-eclampsia and eclampsia. Semin Perinatol 2009;33:130-7.
59. Hofmeyr GJ, Lawrie TA, Atallah ÁN Duley L. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems [review]. Cochrane Database Syst Rev 2010 Aug 4;CD001059.
60. Imdad A, Jabeen A, Bhutta ZA. Role of calcium supplementation during pregnancy in reducing risk of developing gestational hypertensive disorders: a meta-analysis of studies from developing countries. BMC Public Health 2011;11(suppl 3):S18.
61. Duley L, Gülmezoglu AM, Henderson-Smart DJ, Chou D. Magnesium sulphate and other anticonvulsants for women with pre-eclampsia [review]. Cochrane Database Syst Rev 2010 Nov 10;CD000025.
62. Dewey KG, Heinig MJ, Nommsen LA, Peerson JM, Lonnerdal B. Growth of breast-fed and formula-fed infants from 0 to 18 months: the DARLING Study. Pediatrics 1992;89:1035-41.
63. Birch E, Birch D, Hoffman D, Hale L, Everett M, Uauy R. Breast-feeding and optimal visual development. J Pediatr Ophthalmol Strabismus 1993; 30:33-8.
64. Dewey KG, Heinig MJ, Nommsen-Rivers LA. Differences in morbidity between breast-fed and formula-fed infants. J Pediatr 1995;126:696-702.
65. Bhutta ZA, Ahmed T, Black RE, Cousens S, Dewey K, Giugliani E, et al. What works? Interventions for maternal and child undernutrition and survival. Lancet 2008;371:417-40.
66. American AoPWoB. Breastfeeding and the use of human milk. Pediatrics 1997;100:1035-9.
67. Edmond KM, Zandoh C, Quigley MA, Amenga-Etego S, Owusu-Agyei S, Kirkwood BR. Delayed breastfeeding initiation increases risk of neonatal mortality. Pediatrics 2006;117:e380-6.
68. Arifeen S, Black RE, Antelman G, Baqui A, Caulfield L, Becker S. Exclusive breastfeeding reduces acute respiratory infection and diarrhea deaths among infants in Dhaka slums. Pediatrics 2001;108:e67.
69. Dimond HJ, Ashworth A. Infant feeding practices in Kenya, Mexico and Malaysia. The rarity of the exclusively breast-fed infant. Hum Nutr Appl Nutr 1987;41:51-64.
70. Perez-Escamilla R. Breastfeeding in Africa and the Latin American and Caribbean region: the potential role of urbanization. J Trop Pediatr 1994;40:137-43.
71. United Nations Children's Fund. Monitoring the situation of children and women. Infant and Young Child Feeding (2000-2007). http://www.childinfoorg/breastfeeding_countrydataphp. Accessed June 7, 2011.
72. World Health Organization. The optimal duration of exclusive breastfeeding: Report of an expert consultation, Geneva, Switzerland, March 28-30, 2001. Geneva, Switzerland: Department of Nutrition for Health and Development (NHD) and Department of Child and Adolescent Health and Development (CAH); 2001. p. 1-6.
73. Jones DA, West RR. Lactation nurse increases duration of breast feeding. Arch Dis Child 1985;60:772-4.
74. Wright A, Rice S, Wells S. Changing hospital practices to increase the duration of breastfeeding. Pediatrics 1996;97:669-75.
75. Ahluwalia IB, Tessaro I, Grummer-Strawn LM, MacGowan C, Benton-Davis S. Georgia's breastfeeding promotion program for low-income women. Pediatrics 2000;105:E85.
76. Caulfield LE, Gross SM, Bentley ME, Bronner Y, Kessler L, Jensen J, et al. WIC-based interventions to promote breastfeeding among African-American Women in Baltimore: effects on breastfeeding initiation and continuation. J Hum Lact 1998;14:15-22.
77. Morrow AL, Guerrero ML, Shults J, Calva JJ, Lutter C, Bravo J, et al. Efficacy of home-based peer counselling to promote exclusive breastfeeding: a randomised controlled trial. Lancet 1999;353:1226-31.
78. Brent NB, Redd B, Dworetz A, D'Amico F, Greenberg JJ. Breast-feeding in a low-income population. Program to increase incidence and duration. Arch Pediatr Adolesc Med 1995;149:798-803.
79. Aksu H, Kucuk M, Duzgun G. The effect of postnatal breastfeeding education/support offered at home 3 days after delivery on breastfeeding duration and knowledge: a randomized trial. J Matern Fetal Neonatal Med 2011;24:354-61.
80. Renfrew MJ, McCormick FM, Wade A, Quinn B, Dowswell T. Support for healthy breastfeeding mothers with healthy term babies. Cochrane Database Syst Rev 2012 May 16;5:CD001141.
81. World Health Organization. Kangaroo mother care: A practical guide. Geneva: Department of Reproductive Health and Research/WHO; 2003. p. 1-54.
82. Lawn JE, Mwansa-Kambafwile J, Horta BL, Barros FC, Cousens S. 'Kangaroo mother care' to prevent neonatal deaths due to preterm birth complications. Int J Epidemiol 2010;39(suppl 1):i144-54.
83. Bhutta ZA, Khan I, Salat S, Raza F, Ara H. Reducing length of stay in hospital for very low birthweight infants by involving mothers in a stepdown unit: an experience from Karachi (Pakistan). BMJ 2004; 329:1151-5.
84. Afsar FS. Skin care for preterm and term neonates. Clin Exp Dermatol 2009;34:855-8.
85. Darmstadt GL, Dinulos JG. Neonatal skin care. Pediatr Clin North Am 2000;47:757-82.
86. Hammarlund K, Sedin G. Transepidermal water loss in newborn infants. III. Relation to gestational age. Acta Paediatr Scand 1979;68:795-801.
87. Kalia YN, Nonato LB, Lund CH, Guy RH. Development of skin barrier function in premature infants. J Invest Dermatol 1998;111:320-6.
88. Darmstadt GL, Saha SK, Ahmed AS, Ahmed S, Chowdhury MA, Law PA, et al. Effect of skin barrier therapy on neonatal mortality rates in preterm infants in Bangladesh: a randomized, controlled, clinical trial. Pediatrics 2008;121:522-9.
89. Darmstadt GL, Saha SK, Ahmed AS, Choi Y, Chowdhury MA, Islam M, et al. Effect of topical emollient treatment of preterm neonates in Bangladesh on invasion of pathogens into the bloodstream. Pediatr Res 2007; 61:588-93.
90. Edwards WH, Conner JM, Soll RF. The effect of prophylactic ointment therapy on nosocomial sepsis rates and skin integrity in infants with birth weights of 501 to 1000 g. Pediatrics 2004;113:1195-203.
91. Vickers A, Ohlsson A, Lacy J, Horsley A. Massage for promoting growth and development of preterm and/or low birth-weight infants. Cochrane Database Syst Rev 2004;CD000390.
92. van Sleuwen BE, Engelberts AC, Boere-Boonekamp MM, Kuis W, Schulpen TW, L'Hoir MP. Swaddling: a systematic review. Pediatrics 2007;120:e1097-106.