Nutrition and low birth weight: from research to practice¹⁻⁵

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ABSTRACT
Low birth weight (LBW) remains a significant public health problem in many developing countries, and poor nutrition both before and during pregnancy is recognized as an important cause. Emerging evidence on the role of intergenerational effects in determining maternal preconceptual nutritional status indicates the need for continued investment in strategies that improve women’s nutrition and health throughout the life cycle, especially during the early years. Controlled trials have shown that improving food intakes during pregnancy effectively reduces LBW, but programs have been less successful because these interventions are expensive and difficult to manage. Multivitamin-mineral supplements have been viewed as a simpler solution, but 2 of 3 controlled trials conducted to date failed to show that multivitamin-mineral supplements are more effective than iron-folate supplements, which are already the standard of care during pregnancy. Emerging evidence indicating the benefits of iron supplements in improving birth weight illustrate the need for increased efforts to reduce iron deficiency by improving coverage of antenatal programs and promoting fortification. Other causes of LBW include environmental factors, such as smoking; indoor air pollution; and infections, such as malaria. However, little is known about the interactions between nutrition and infection. Underlying social factors, such as poverty and women’s status, are also important, especially in South Asia, where more than one-half of the world’s LBW infants are born. In summary, strategies that combine nutrition-based interventions, such as improving food intakes and micronutrient status, especially iron status, with approaches that improve women’s status and reproductive health are needed to reduce LBW.  


KEY WORDS Nutrition, low birth weight, intergenerational effects, intervention strategies, micronutrients, iron

INTRODUCTION
Low birth weight (LBW), defined as a birth weight <2500 g, remains a significant public health problem in many parts of the world and is associated with a range of both short- and long-term adverse consequences. Although about one-half of all LBW infants in industrialized countries are born preterm (<37 wk gestation), most LBW infants in developing countries are born at term and are affected by intrauterine growth restriction that may begin early in pregnancy (1). The latest regional estimates of LBW (Figure 1) range from 25% in South Asia, where more than one-half of the world’s LBW infants are born, to 10% and 12% in Sub-Saharan Africa and Latin America, respectively (2). Although these rates are higher than the goal of <10% that was established by world leaders at the 1990 World Summit for Children, the data for examining trends in developing countries are limited and of questionable quality when available. More than two-thirds of births are not reported in many parts of Africa, Asia, and Latin America, because many deliveries occur in homes or small health clinics (2). This may result in an underestimation of the prevalence of LBW, because lower-income, higher-risk groups may be the least likely to be included in hospital- or urban-based data sets.

Nevertheless, it is plausible that improvements may have occurred in some regions. We have more reliable data indicating reductions in the prevalence of early childhood malnutrition in some regions, suggesting possible declines in LBW (3). This is further corroborated by data indicating improved food security, improved maternal nutritional status, favorable demographic changes, and increased access to antenatal care. This article focuses on recent advances in the study of the role of nutrition in reducing LBW, both in research and programmatic settings.

ROLE OF NUTRITION
Poor nutrition is a known cause of LBW, especially in developing countries. In his classic review published more than a decade ago, Kramer (4) concluded that maternal nutritional factors both before and during pregnancy account for >50% of cases of LBW in many developing countries (Figure 2). Most of this evidence was based on pre-pregnancy nutritional status assessed by using anthropometric criteria and the adequacy of energy and protein intakes during pregnancy. Maternal...
prepregnancy size is a well-known determinant of birth size. On the basis of a large meta-analysis of data from >100 000 women from all over the world, the World Health Organization Collaborative Study concluded that prepregnancy weight predicted the risk of LBW with an odds ratio (per unit decrease in prepregnancy weight) of >2 (Table 1). Other indicators that predicted risk included maternal height, prepregnant body mass index, and midupper arm circumference (5).

The key questions, however, are when and how to improve preconceptual nutritional status. It is in this context that understanding the intergenerational nature of growth failure (Figure 3) becomes important. The classic pattern in many developing countries is that infant girls born with LBW continue to experience growth failure during early childhood and perhaps adolescence, most likely have children at an early age (which further reduces their opportunity to reach an optimal body size with adequate nutrient stores before conception), and thereby give birth to LBW infants (6).

Recent data from long-term studies in Guatemala provide evidence for the role of such intergenerational effects (7–10). A series of studies have been conducted over the past 30 y by the Instituto de Nutricion de Central America y Panama (INCAP) in 4 villages of eastern Guatemala. The first study was a longitudinal, community-based, food supplement trial conducted between 1969 and 1977. Four villages, stratified by size, were randomly assigned to receive either a high-energy, high-protein supplement (containing 91 kcal and 6.4 g protein/100 mL) or a low-energy, no-protein drink (containing 33 kcal/100 mL). Both supplements were fortified with vitamins and minerals. The target population of the intervention was pregnant and lactating women and children aged ≤7 y, and consumption was ad libitum (11).

In the 1990s, our group at Emory University, led by Dr Martorell, in collaboration with INCAP, returned to these villages and followed up on the pregnancy outcomes of many of the women who had participated as young children in the original intervention trial. We found significant differences in the birth weight of the next generation on the basis of the type of supplement the mothers were exposed to in their early years (12). We have also shown differences based on the level of childhood growth retardation by using stunting at 3 y as a key indicator (13). There was a difference of almost 150 g in the birth weight of the next generation (mean birth weight: 2988 g) when we compared the 2 extremes, ie, women who were severely stunted and women who were mildly stunted as young children. We have also found strong intergenerational relations in birth weight and length that are almost twice as large as those reported for developed countries, where most such studies have been carried out to date (7). Although these intergenerational effects reflect both genetic and environmental influences across generations, they do suggest that environmental influences may be much greater in poor settings. In summary, these findings explain why it may take longer to reduce LBW.

Nevertheless, we must focus on what we can do now. Improving dietary intakes during pregnancy is an obvious solution. However, the results of our efforts in doing this through either behavior change or provision of food supplements are not encouraging. It is important to note that the results of several efficacy trials have shown that food supplementation during pregnancy improves birth weight. On the basis of a meta-analysis of controlled trials, Kramer (14) concluded that balanced protein-energy supplements during pregnancy can reduce the incidence of small-for-gestational-age infants by almost one-third (Table 2). In particular, the study by Cessey et al (15) in The Gambia showed significant reductions in both

![FIGURE 2. Determinants of low birth weight (LBW) in developing countries (4). A plus sign indicates a nutritional factor. The key to the shading starts with the arrow indicating short stature and runs clockwise.](#)

![FIGURE 3. Intergenerational cycle of growth failure (6).](#)

<table>
<thead>
<tr>
<th>Indicator</th>
<th>LBW</th>
<th>IUGR</th>
<th>Preterm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (cm)</td>
<td>1.7</td>
<td>1.9</td>
<td>1.2</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>2.3</td>
<td>2.5</td>
<td>1.4</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>1.8</td>
<td>1.8</td>
<td>1.3</td>
</tr>
<tr>
<td>Midupper arm circumference (cm)</td>
<td>1.9</td>
<td>1.6</td>
<td>1.2</td>
</tr>
</tbody>
</table>

1 Odds ratios are presented for each outcome per unit decrease in each indicator. From reference 5.
**NUTRITION AND LOW BIRTH WEIGHT**

### TABLE 2
Summary of controlled trials of prenatal balanced protein-energy supplements and small-for-gestational-age (SGA) births

<table>
<thead>
<tr>
<th>Study site and year</th>
<th>Sample characteristics</th>
<th>Study design</th>
<th>Odds ratio (95% CI) for SGA births</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Subjects</td>
<td>n</td>
<td>Intervention</td>
</tr>
<tr>
<td>Taiwan (1973)</td>
<td>Well-nourished pregnant women</td>
<td>182</td>
<td>800 kcal + 40 g protein + vitamins, minerals</td>
</tr>
<tr>
<td>Columbia (1980)</td>
<td>Poor urban women in third trimester</td>
<td>456</td>
<td>865 kcal + 38 g protein</td>
</tr>
<tr>
<td>United States (1980)</td>
<td>High-risk African American pregnant women</td>
<td>529</td>
<td>322 kcal + 6 g protein</td>
</tr>
<tr>
<td>Wales (1981)</td>
<td>Well-nourished pregnant women</td>
<td>1251</td>
<td>Tokens for free milk</td>
</tr>
<tr>
<td>India (1984)</td>
<td>Poor, malnourished pregnant women in third trimester</td>
<td>20</td>
<td>417 kcal + 30 g protein</td>
</tr>
<tr>
<td>The Gambia (1997)</td>
<td>Chronically malnourished rural women (20 wk gestation)</td>
<td>2047</td>
<td>1017 kcal + 22 g protein + Ca, Fe</td>
</tr>
</tbody>
</table>

† From reference 14. The summary estimate (95% CI) was 0.64 (0.53, 0.78).

LBW and neonatal mortality, especially during periods of low food intake and high energy expenditure. Programmatic evidence is limited, however, and the high cost of these programs is a concern.

Several factors, such as poverty, women’s status, and cultural beliefs and practices, may act as barriers to successful programs. Poverty acts to limit access to care and the choice and amount of foods available to pregnant women. Women’s status may influence pregnancy weight gain through the family’s response to the woman’s pregnancy. It is in this context that the potential of using micronutrient supplements rather than food became attractive to many international agencies in the 1990s (16). Micronutrient supplements are cheaper and more feasible and can improve dietary quality by providing several key nutrients, such as iron, vitamin A, folate, and zinc, at the same time. The findings from Tanzania by Fawzi et al (17) were also highly encouraging. This was a controlled trial among HIV-infected but asymptomatic women. The prevalence of LBW was only 9% in the 2 groups who received multivitamins with or without vitamin A, compared with 14.5% and 17.2% for those who received iron-folate and vitamin A and iron-folate only, respectively.

At the same time, our group at Emory University conducted a randomized double-blind trial in semirural Mexico in which we evaluated the effect of prenatal multiple micronutrient supplements compared with that of a standard iron supplement. This was a collaborative effort between Emory University and the Instituto Nacional de Salud Publica in Cuernavaca, Mexico. Women were recruited early in their pregnancy and were allocated to receive either multiple micronutrient supplements that contained 1–1.5 times the recommended dietary allowance of key vitamins and minerals including 60 mg Fe (MM group) or supplements containing only 60 mg Fe (Fe group), which was the standard treatment at that time. The supplements were distributed 6 d/wk by trained workers, who administered and recorded consumption. The main outcomes were birth size and gestational age. Data were also collected on micronutrient status, dietary intakes, and anthropometric indexes during pregnancy and early postnatal life. A total of 921 pregnant women were identified, of whom 873 were assigned to treatment after determining eligibility and obtaining informed consent. Data on birth outcomes were available for 656 pregnancies, and comparisons by intervention group were done for 645 singleton live births. Loss to follow-up was ~25% and was similar in both groups. These rates were high because of the early recruitment. Comparison of several baseline characteristics between the 2 groups showed that the groups did not differ significantly in age, parity, or hemoglobin concentrations, but women in the Fe group were significantly heavier than were those in the MM group. There were no significant differences in the main outcomes of interest—birth weight, length, ponderal index, and gestational age—by intervention group, and these findings did not change even after adjustment for baseline differences in maternal body mass index. Mean birth weights were 2981 ± 391 and 2977 ± 393 g in the MM and Fe groups, respectively (18).

The findings of our study were indeed contrary to the expectation that multivitamin-mineral supplements would improve birth size when compared with routine iron supplementation. The absence of effect was not due to factors such as inadequate sample size or poor compliance. However, the prevalence of LBW was lower than originally expected, and it is also possible that zinc, which was shown to not improve birth size (19, 20), may have interacted with other nutrients in the supplement. Our findings do suggest that multivitamin-mineral supplements are safe, and we are currently examining other benefits, such as improved maternal and child nutrition, in our ongoing studies of child growth and development in this study population.

Without doubt, the results of other similar trials conducted in different study settings are needed before conclusions can be reached. It is in this context that the recently published findings from a similar trial in rural Nepal are interesting (21). Although this study had several treatment groups, there was no additional benefit of multivitamin-mineral supplements in reducing LBW when compared with standard iron-folate supplements, despite the high rates of LBW and micronutrient malnutrition. Of note is that LBW was significantly lower in the group who received iron-folate supplements along with vitamin A (34.3%) than in the control group, who received only vitamin A (43.4%). A controlled trial by Cogswell et al (22) also showed the benefits of iron supplements in reducing LBW, even among nonanemic pregnant women in the United States; in that study, the incidence of LBW was 5% and 14% for the iron and placebo groups, respectively. These findings clearly illustrate the importance of iron in reducing LBW, in contrast with earlier
concerns about lack of evidence from well-controlled trials (23), and call for more attention to programs to improve iron status. It is noteworthy that the lower-than-expected rates of LBW in the Mexico study may have been the result of high compliance (>85%) with iron supplementation during pregnancy.

Anemia, which is mostly due to iron deficiency in many parts of the world, is a problem in the same places where LBW is a concern (24, 25). Although the data are limited, rates of anemia have not declined among both pregnant and nonpregnant women in most developing countries (25). Despite official reports of high coverage of iron supplementation programs, problems such as inadequate supply and poor quality of iron supplements and poor compliance are common in many antenatal care programs. Poor provider and consumer education also needs to be addressed (26). Another issue is that pregnancy may be too narrow a window to improve iron status, and efforts to include all women of reproductive age are needed. It is in this context that fortification of staple foods such as flour offers promise. Fortification of flour with iron and other nutrients has been in place in many industrialized countries and is widespread in the Americas. Data from the National Health and Nutrition Examination Surveys in the United States clearly illustrate the role of iron supplements and fortified foods in improving iron status among women of reproductive age (27). Similarly, significant reductions in iron deficiency anemia have been attributed to the fortification of flour in Chile and Venezuela (28). The challenge, however, is to extend this knowledge to the parts of the world that need it most. There are several hurdles to cross, such as establishing effective collaboration between the public and private sectors, monitoring and evaluation, quality control, regulation, and legislation, appropriate targeting, and inadequate regional and local expertise.

**ROLE OF OTHER FACTORS**

Finally, it would be remiss to assume that nutrition is the only cause of LBW. The etiology of LBW is complex and may vary by setting. Several nonnutritional factors, such as infections, hypertension, smoking, and environmental factors (such as indoor air pollution due to cooking smoke and poor housing quality) are known determinants (29). The role of infections in particular is interesting; for example, malaria prophylaxis may not cause LBW in primigravida (30). However, little is known about the interaction of these factors with nutrition during pregnancy, despite awareness of the role of the interaction between nutrition and infection in child health and nutrition (31).

Last, we cannot ignore the role of underlying factors such as poverty and women’s status. Poor women’s status, which includes inequity in both social status and physical and mental well-being, is especially important in South Asia, where more than one-half of the world’s LBW infants are born. In their well-known paper on the “Asian enigma,” Ramalingaswami et al (32) proposed poor women’s status as the main reason for higher rates of malnutrition in South Asia than in Sub-Saharan Africa despite better indicators of food security and gross domestic product in the former. By using data from the Demographic Health Surveys, we were able to show a strong relation between women’s decision making and their children’s weight-for-age and that women’s status was important in both regions but mattered more in South Asia (33).

**TABLE 3**

Comparison of women’s health and nutrition in South Asia with that in Sub-Saharan Africa

<table>
<thead>
<tr>
<th></th>
<th>South Asia</th>
<th>Sub-Saharan Africa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stunting (%)</td>
<td>16</td>
<td>3</td>
</tr>
<tr>
<td>Underweight (%)</td>
<td>60</td>
<td>20</td>
</tr>
<tr>
<td>Thinness (%)</td>
<td>40</td>
<td>20</td>
</tr>
<tr>
<td>Anemia (%)</td>
<td>63</td>
<td>50</td>
</tr>
<tr>
<td>Age at first marriage (y)</td>
<td>17.1</td>
<td>17.3</td>
</tr>
<tr>
<td>Fertility rate (no. of births/woman)</td>
<td>3.5</td>
<td>5.9</td>
</tr>
<tr>
<td>Prenatal care (%)</td>
<td>56</td>
<td>80</td>
</tr>
<tr>
<td>Birthing care (%)</td>
<td>22</td>
<td>41</td>
</tr>
</tbody>
</table>

* From references 25 and 33.

In conclusion, there is agreement on effective strategies that need to be pursued with innovative thinking and persistence. In the area of nutrition, there is an urgent need to identify and pursue strategies to improve both food intakes and micronutrient status, especially iron status, before and during pregnancy. The importance of intergenerational effects further justify the need for sustained efforts that will improve women’s health and nutritional status over at least a couple of generations. Equally important are the role of reproductive health strategies, such as increasing the age at marriage and birth spacing, and finding ways to improve women’s status. The real challenge, however, is to improve program delivery and to integrate services. For example, iron supplements are typically distributed by the reproductive health sector, who often do not recognize or even value the importance of the supplements. Similarly, efforts to improve food intakes may be more effective if they are combined with strategies that address underlying factors such as poverty and women’s status. Finally, the search for new solutions, eg, the role of long-chain polyunsaturated fatty acids and the interaction between nutrition and infection, should be pursued while we strive to improve the effectiveness of existing programs.
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