Maternal Nutrition Interventions to Improve Maternal, Newborn, and Child Health Outcomes

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Abstract

Maternal undernutrition affects a large proportion of women in many developing countries, but has received little attention as an important determinant of poor maternal, newborn, and child health (MNCH) outcomes such as intrauterine growth restriction, preterm birth (PTB), and maternal and infant morbidity and mortality. We recently evaluated the scientific evidence on the effects of maternal nutrition interventions on MNCH outcomes as part of a project funded by the Gates Foundation to identify critical knowledge gaps and priority research needs. A standardized tool was used for study data abstraction, and the effect of nutrition interventions during pregnancy or of factors such as interpregnancy interval on MNCH outcomes was assessed by meta-analysis, when possible. Several nutrient interventions provided during pregnancy have beneficial effects on MNCH outcomes, but are not widely adopted. For example, prenatal calcium supplementation decreases the risk of PTB and increases birthweight; prenatal zinc, omega-3 fatty acids and multiple micronutrient supplements reduce the risk of PTB (<37 weeks), early PTB (<34 weeks) and low birthweight (LBW), respectively. Among currently implemented interventions, balanced protein-energy and iron-folic acid supplementation during pregnancy significantly reduce the risk of LBW by 20–30% in controlled settings, but variable programmatic experiences have led to questionable effectiveness. Early age at pregnancy and short interpregnancy intervals were also associated with increased risk of PTB, LBW and neonatal death, but major gaps remain on the role of women’s nutrition before and during early pregnancy and nutrition education and counseling. These findings emphasize the need to examine the benefits of improving maternal nutrition before and during pregnancy both in research and program delivery.
Introduction

Maternal, newborn, and child health (MNCH) outcomes such as anemia, intrauterine growth restriction (IUGR), low birthweight (LBW), and preterm birth (PTB) remain major public health problems that are associated with significant costs to health care and human capital formation [1]. Preeclampsia, one of the leading causes of maternal morbidity and mortality worldwide, can lead to poor health outcomes for both the mother (e.g. damage to vital organs) and her child (e.g. IUGR, PTB) [2]. Although considerable strides and investments have been made in improving child health and survival, the importance of maternal and child nutrition especially during the first 1,000 days that begin in utero through the first year of life has received attention only recently [3, 4]. Maternal nutrition before and during pregnancy is especially important for healthy pregnancy outcomes in many lower and middle-income countries (LMIC), where women enter pregnancy undernourished and their nutritional status worsens throughout pregnancy due to the increased demand for nutrients [5]. For example, anemia is widespread among women of reproductive age in many LMIC. Anemia during pregnancy, especially severe anemia which is often due to iron deficiency, has been linked to poor health outcomes such as LBW, PTB, maternal morbidities, and maternal and child mortality [6]. Several public health programs have strived to reduce the prevalence of anemia, especially in high-risk areas, but these efforts have not translated to improved outcomes often due to poor program implementation and/or inadequate support for maternal health. Inadequate food intake in terms quantity and quality combined with high prevalences of underweight and/or short stature has also been associated with poor MNCH outcomes in some settings [7, 8].

This review examines the state of current knowledge on the impact of nutrition-related interventions for women before and during pregnancy on MNCH outcomes including IUGR, LBW, PTB, newborn and child growth, morbidity and mortality, and maternal morbidity and mortality with recommendations for programs and research.

Methods

We based the present review on a recently published collection of meta-analyses examining the effect of maternal nutrition on a broad range of MNCH outcomes, with a particular focus on nutrition interventions during pregnancy [9]. The meta-analyses describe interventions during pregnancy, pre-pregnancy interventions, and nutrition throughout the life cycle. Authors conducted the meta-analyses and comprehensive literature reviews using evidence from randomized controlled trials (RCTs) and/or observational studies. Although the meta-analyses primarily focused on nutrition interventions during preg-
nancy, the topics of antihelminthics in pregnancy, nutrition education and counseling, household food production, short interpregnancy interval, early age at first childbirth, nutrition before and during pregnancy, and intergenerational influences on child growth and undernutrition were included because of their potential impact on maternal and child health outcomes [10–16]. We reviewed meta-analyses of the following specific supplementation trials during pregnancy: iron or iron + folic acid (IFA), vitamin A, select B vitamins, vitamin D, n-3 long-chain polyunsaturated fatty acids (n-3 PUFA), iodine, zinc, calcium, multiple micronutrient (MMN), balanced protein-energy, and antihelminthics [10, 17–27]. For all reviews, authors abstracted study data using a standardized Excel-based tool that captured information on 49 potential variables, for example sample size, study design, study context, and estimated effect [9]. Authors graded the quality of evidence for each intervention, where data were available, using the Child Health Epidemiology Reference Group’s (CHERG) adaptation of the GRADE methodology as a guide [28, 29].

### Results

The results of findings for nutrition interventions during pregnancy and nutrition-sensitive interventions before and during pregnancy are described in the following sections.

#### Nutrition Interventions during Pregnancy

A summary of the number of individual trials included in the meta-analyses of nutrition interventions during pregnancy is given by type of intervention and outcome in table 1. The number of trials ranged from 0 to 20 and varied by type

| Table 1. Number of prenatal nutrition intervention trials included in each meta-analysis, by intervention and outcome |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Calcium | Iodine | Iron or IFA | Zinc | Vit A | Vit D | Vit B₆ | Vit B₁₂ | Vit C (+E) | n-3 PUFA | MMN | Balanced protein-energy |
| PTB | 11 | – | 12 | 16 | 7 | 2 | – | – | 9 | 9 | 9 | 6 |
| LBW | 6 | – | 11 | 11 | 5 | 3 | – | – | 5 | 8 | 15 | 5 |
| Birthweight | 13 | 2 | 13 | 20 | 7 | 5 | 3 | – | 8 | 9 | 14 | 16 |
| Neonatal or infant mortality | 2 | 2 | 4 | – | 5 | – | – | – | 9 | 6 | 9 | 3 |
| Anemia | – | – | 18 | – | 8 | – | – | – | – | – | 7 | – |
| PIH or preeclampsia | 15 | – | 2 | – | – | 2 | – | – | 9 | 4 | – | 3 |
| Maternal mortality | – | – | – | – | 3 | – | – | – | – | – | 2 | – |

Dashes indicate not reported or very low-quality/insufficient data. PIH = Pregnancy-induced hypertension.
of intervention and outcome measured. Several trials were identified for interventions such as zinc, calcium, IFA, MMN and balanced protein-energy. In contrast, there have been no trials of vitamin B₁₂ supplementation during pregnancy, and very few trials of prenatal vitamin B₆, vitamin D, and iodine supplementation. The majority of included trials reported more information on newborn outcomes such as LBW, birthweight, and PTB than on maternal outcomes. There were also differences in the nature of the intervention received by the treatment and control groups, especially for the trials that evaluated mult nutrient interventions. The MMN trials used IFA as the control group, and the authors defined MMN as 5 or more micronutrients. A mix of interventions and controls were used in the balanced protein-energy trials (e.g. in some trials both groups received micronutrients, in other trials only the intervention group received micronutrients), and zinc was often provided in addition to other micronutrients (e.g. zinc + MMN vs. MMN alone). Vitamins C and E were given concurrently in the included vitamin C trials.

Table 2 lists key results on the effect of maternal nutrition interventions on newborn outcomes. Supplementation with calcium, balanced protein-energy, MMN, IFA, or n-3 PUFA resulted in a significant (p < 0.05) mean increase in birthweight, compared to controls (42–86 g higher). Babies born to mothers supplemented with IFA, MMN, or balanced protein-energy had a lower risk of being born LBW than controls. Calcium and zinc supplementation significantly decreased the risk of PTB (<37 weeks), while n-3 PUFA supplementation decreased the risk of early PTB (<34 weeks). Prenatal supplementation with vitamin A decreased the risk of LBW in a subpopulation of HIV+ women (RR: 0.79,
95% CI: 0.64–0.99; data from 3 RCTs), but no significant effect was found in the total population [18]. High-quality evidence demonstrates that prenatal iodine supplementation decreased the risk of cretinism (RR: 0.27, 95% CI: 0.12–0.60; data from 5 RCTs) and improved developmental scores (data from 4 RCTs) in children born to mothers at risk of iodine deficiency [22]. Evidence also suggests that prenatal iodine supplementation decreased the rate of infant mortality (data from 2 RCTs, total n = 37,400). Supplementation with vitamin B₆ resulted in higher mean birthweight; however, small sample size and poor study quality render this estimate unreliable [19].

Table 3 shows key, though limited, results of the effect of nutrition interventions on maternal health outcomes. Of note, calcium supplementation decreased the risk of preeclampsia, pregnancy-induced hypertension, and maternal mortality/severe morbidity [24]. Iron or IFA and vitamin A significantly decreased the risk of maternal anemia [17, 18], but MMN interventions did not further reduce the risk of anemia compared to IFA [27]. We did not find any evidence of benefit for maternal mortality that was based on fewer trials (n = 5) that examined the effects of vitamin A (RR: 0.86, 95% CI: 0.6–1.24; 3 trials) and MMN interventions (RR: 0.96, 95% CI: 0.64–1.45; 2 trials) [18, 25].

Nutrition-Related Factors before and during Pregnancy

These topics include nutrition education and counseling during pregnancy, household food production strategies, increasing interpregnancy interval, early age at first childbirth and women’s nutritional status before and during early pregnancy. Data from well-controlled trials were limited for many of these out-
comes. In cases where it was not possible to conduct an RCT due to the nature of the topic, authors used data from high-quality observational studies to conduct meta-analyses. Authors carried out a meta-analysis of antihelminthics during pregnancy; however, few RCTs have been conducted. The topics of preconception nutrition intergenerational influences on child growth and nutrition were presented as reviews.

Table 4 shows results from the meta-analyses of factors that may influence MNCH outcomes. Antihelminthics in pregnancy reduced the risk of very LBW; however, the meta-analysis included only 2 trials (1,936 women). Nutrition education and counseling resulted in improvements in various MNCH outcomes (anemia, PTB and birthweight). Early age at first childbirth and short interpregnancy interval significantly increased the odds of PTB and LBW. Early age at first childbirth also resulted in increased odds of stillbirth (aOR: 1.35, 95% CI: 1.07–1.71) and early neonatal death (aOR: 1.29, 95% CI: 1.02–1.64) [8]. Four studies examining household food production strategies as a means to improve nutritional status focused mainly on child malnutrition as an outcome and found no effect on stunting, underweight, or wasting [11]. The analyses of nutrition education and counseling, household food production strategies, short interpregnancy interval, and early age at first childbirth

<table>
<thead>
<tr>
<th></th>
<th>Anemia</th>
<th>PTB</th>
<th>LBW</th>
<th>Birthweight, g</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>trials or studies (total)</td>
<td>pooled RR or aOR (95% CI)</td>
<td>trials or studies (total)</td>
<td>pooled RR or aOR (95% CI)</td>
</tr>
<tr>
<td>Antihelminthics</td>
<td>3 (2,035)</td>
<td>0.93 (0.79–1.10)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Nutrition education and counseling</td>
<td>11 (2,588)</td>
<td>0.70 (0.58–0.84)</td>
<td>10 (3,384)</td>
<td>0.81 (0.66–0.99)</td>
</tr>
<tr>
<td>Short interpregnancy interval</td>
<td>–</td>
<td>–</td>
<td>6 (126,863)</td>
<td>1.41 (1.20–1.65)</td>
</tr>
<tr>
<td>Early age at first childbirth</td>
<td>8 (36,197)</td>
<td>1.36 (1.24–1.49)</td>
<td>23 (310,702)</td>
<td>1.68 (1.34–2.11)</td>
</tr>
</tbody>
</table>

Dashes indicate not reported or very low-quality/insufficient data.

1 Estimates presented in this table are of moderate to low quality due to the heterogeneity of study design and analytical methods.
2 Very LBW.
3 Interpregnancy interval <6 months.
included studies that varied in quality and were quite methodologically heterogeneous.

The review on the role of women’s nutrition before and during pregnancy found high-quality evidence supporting the importance of folate during the periconceptional period in reducing the risk of neural tube defects and suggestive of reductions for other birth defects such as congenital anomalies. The evidence from observational studies that examined women’s nutritional status based on anthropometry and/or micronutrient status suggests possible benefits for outcomes such as PTB and LBW, but the studies were of poor quality, and there were no well-designed trials [15]. In contrast, evidence from long-term follow-up studies strongly supports that investing in strategies to improve child nutrition during the first few years of life results in improved maternal nutritional status later on, which may be linked to improved birth outcomes for the next generation [16].

**Discussion and Conclusions**

We reviewed results from a recent collection of meta-analyses examining the role of maternal, and especially prenatal, nutrition interventions on MNCH outcomes [9]. Meta-analyses of intervention trials showed that prenatal supplementation with calcium, IFA, n-3 PUFA, MMN, or balanced protein-energy resulted in higher mean birthweight, compared to controls. Prenatal supplementation with calcium, zinc, and n-3 PUFA also lowered the risk of PTB, and iron, MMN, and balanced protein-energy supplementation resulted in a lower risk of LBW. There was strong evidence that prenatal calcium supplementation decreased the risk of preeclampsia, and that IFA supplementation decreased the risk of anemia. Nutrition education and counseling during pregnancy is a promising strategy to improve maternal nutrition, although more well-designed studies are needed to estimate the cost-effectiveness and barriers to implementation of this public health strategy. Analysis of observational study data for the topics of nutrition education and counseling, household food production strategies, interpregnancy interval, and early age at first childbirth was more often than not limited by heterogeneity of study design and analytical methodology.

This review helped identify existing interventions that work and need to be strengthened with improved program implementation, new interventions that are efficacious but not widely implemented, and finally important gaps that need to be addressed in future research to generate findings that will help guide policy and programs. The provision of iodine using iodized salt and/or supplements
is the most successful intervention to date, but constant monitoring is still needed. Balanced protein-energy and IFA supplementation during pregnancy are also important existing interventions that can significantly improve MNCH outcomes but face programmatic challenges. Solutions to address barriers related to program delivery, costs and scaling up are needed to improve effectiveness in settings where food insecurity and poor access to care are common. Innovative approaches that evaluate targeting, nutrition education and cash transfer programs should be pursued.

The interventions that have promise for future implementation are the provision of MMN supplements, calcium and omega-3 fatty acids during pregnancy, but these interventions need more testing in programmatic settings in LMIC. MMN interventions are safe and efficacious, but earlier concerns about possible adverse effects on neonatal mortality and issues related to the dose and composition of these supplements remain hurdles to implementation. Calcium supplementation shows evident benefit in trials, and implementation research is urgently needed given that the problem of preeclampsia is serious and widespread in both developing and developed countries. In the case of omega-3 fatty acids, most of the research has been done in developed countries rather than LMIC, where the impact of supplementation may be greater. Hence, more n-3 PUFA supplementation trials are needed in LMIC. Cost-effective ways of delivering the above interventions are also needed.

Finally, this review also identified major research gaps as outlined below:

- Dearth of evidence on several maternal outcomes
- Few antihelminthics trials – this is unfortunate because this problem is widespread in many regions of the world and the intervention is amenable to an RCT design
- More rigorous, controlled, balanced protein-energy trials also including micronutrients, fatty acids, etc. (i.e. fortified foods) and/or nutrition counseling should be considered along with additional outcomes
- Well-designed observational studies that examine the relationships between pre-pregnancy body size and composition and MNCH outcomes are needed
- The relationships between nutrition and infection during early pregnancy for predicting subsequent outcomes is unclear
- Efficacy of balanced protein-energy and/or micronutrient interventions (IFA, MMN) before and during early pregnancy on MNCH outcomes

Future research that evaluates the benefits of improving women’s nutrition before and during pregnancy is critical to having better informed strategies that will help reduce the burden of outcomes such LBW, PTB and maternal and neonatal mortality, especially in settings where underlying issues such as poverty, food insecurity and gender discrimination remain.
Disclosure Statement

The authors declare that no financial or other conflict of interest exists in relation to the content of the chapter.

References


