Linking maternal and infant benefits of a nutritional supplement during pregnancy and lactation¹⁻³

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ABSTRACT To evaluate the effect of a nutritional supplement on change in women’s weight during a reproductive cycle and on the difference in birth weight between one infant and the previous one, we analyzed data on 176 complete reproductive cycles from an experiment that was conducted in rural Guatemala. Women with an initial weight <50 kg were classified as marginally nourished or malnourished. Women whose intake of the supplement was in the top 2 tertiles were distinguished from those whose intake was in the lowest tertile. Linear regression modeling was used to estimate the effect of supplementation on these outcomes and to control for confounding factors. Malnourished women gained weight during the reproductive cycle, but their second (study) infant tended to weigh less at birth than their prior-born infant. Higher intakes of supplement were associated with a less negative difference in birth weight. Marginally nourished women lost weight during the reproductive cycle and their second (study) infant tended to weigh more at birth than their prior-born infant. Higher intakes of supplement were associated with a less negative difference in birth weight trend for the women themselves. Well-nourished women and their infants did not show any of these benefits from supplementation. These findings help explain past contradictory findings on maternal depletion as well as on the benefits of nutritional supplementation for mothers and their infants. Am J Clin Nutr 1998;68:656–61.

KEY WORDS Nutritional supplement, benefit, women, birth weight, reproduction, weight, infants, Guatemala, atole, fresco

INTRODUCTION

How important is maternal health for infant health and how much does childbearing pattern affect maternal health? Knowledge in these 2 areas is crucial for the design of programs to promote optimal maternal and child health. Many studies have shown an association between maternal characteristics and rates of stillbirth, premature delivery, low birth weight, and poor infant growth (1, 2). The maternal characteristics include nutritional status, infections, birth spacing, parity, and workload. However, the relative importance of these characteristics varies in different settings and their mechanisms are not fully understood. For example, the association between maternal dietary intake, through maternal nutritional status, and infant birth weight has been called into question (3). One careful review even concluded that there is little benefit to either mother or child of a nutritional supplement provided to the mother during pregnancy (4). Of studies evaluating the effect of repeated, closely spaced childbearing on women’s health (so-called maternal depletion), support exists for negative as well as positive effects of higher parity and shorter birth intervals on maternal nutritional status (5, 6). However, the ability of these studies to capture the cost of childbearing on women’s health has been questioned (5, 6).

We have suggested that studies of maternal depletion should evaluate overall change in maternal nutritional status across a full reproductive cycle, in conjunction with changes in birth weight and nutritional status between the 2 siblings born during that cycle (7). In applying this framework to a Pakistani population (8), we found that malnourished women experienced a net weight gain during the reproductive cycle concurrent with a negative trend in infant birth weight. In contrast, marginally nourished women lost weight during the reproductive cycle concurrent with a positive trend in infant birth weight. For well-nourished women, there was little net change in either maternal weight or infant birth weight. Likewise, Kusin et al (9) reported that Indonesian women who suffered from chronic energy deficiency experienced net weight increases 1 and 12 mo after the first observed pregnancy as well as 1 and 12 mo after the next pregnancy. Less than optimal infant birth weight and growth were also observed. In contrast, well-nourished women experienced little net change in...
weight over the same period, and infant birth weight and growth were adequate. Furthermore, studies from Taiwan (10), the Philippines (11), Bangladesh (12), and Mexico and Kenya (13) reported lower initial maternal weight-for-height or less initial subcutaneous fat to be associated with larger gains in maternal weight or subcutaneous fat during periods within a reproductive cycle.

These findings reflect results that we showed previously in experimental animals (14). Rats were fed ad libitum or 75% or 60% of the food intake of their ad libitum-fed counterparts during a reproductive cycle. During full lactation, all animals lost weight; the 2 food-restricted groups lost more weight than the ad libitum–fed controls. During the period of partial lactation and non-pregnancy and nonlactation, the most food-restricted rats gained a modest amount of weight, whereas the ad libitum–fed rats lost a substantial amount of weight. The increase in birth weight in pups from the first to the second litter was much larger for the litters of the control than of the food-restricted group (15).

Together, these studies indicate a different partitioning of nutrients between mothers and their offspring, depending on the initial nutritional status of the mother. This may explain earlier contradictory findings on maternal depletion and benefits of maternal nutritional supplementation. On the basis of our prior results, we expected maternal response to a nutritional supplement to depend on the mother’s initial nutritional status because the partitioning of benefits between mother and child varies depending on the initial nutritional status of the mother.

We evaluated the simultaneous benefits to mother and infant during a full reproductive cycle of a maternal nutritional supplement, adjusting for initial maternal nutritional status. Inferences from these results will be important to our understanding of the partitioning of nutrients between mother and child as well as to our determining appropriate nutrition interventions in malnourished populations.

SUBJECTS AND METHODS

Study setting

Data from a nutrition supplementation trial conducted by the Institute of Nutrition of Central America and Panama (INCAP) in Guatemala (1969–1977) were used to investigate the effect of mild-to-moderate protein-energy malnutrition on child growth and mental development. A high-energy, high-protein beverage (atole) was provided in 2 villages and a low-energy, no-protein drink (fresco) was provided in 2 comparable villages. In 1975, the 4 villages combined had a total population of 3359. The energy and protein contents of atole were 3.80 MJ/L and 64 g protein/L, respectively. The energy content of fresco was 1.40 MJ/L. Both supplements had similar concentrations of those micronutrients that may have been inadequate in the home diets. The supplements were available to all villagers midmorning and midafternoon in a central location in these small villages. For pregnant and lactating women, individual intakes of supplement were measured daily to the nearest 10 mL. In addition, preventive and curative medical care were provided to all villagers. The study is described in further detail elsewhere (16); however, the finding of major relevance to the present research was that birth weight was related to energy intake from the supplement.

Supplemental protein made no additional contribution to birth weight (17).

Measurements

In the present study, maternal body measurements were obtained every 3 mo during pregnancy, at delivery, and at 3, 6, 9, and 12 mo postpartum. Change in energy status over one reproductive cycle (from one delivery to the next consecutive delivery) was estimated by change in maternal weight ($\Delta W$; weight 3 mo postpartum of second child – weight 3 mo postpartum of first child). Infant weights were recorded within 24 h after each delivery. Trends in birth weight ($\Delta BW$) were calculated as the difference in birth weight between the second and first study infants for each woman.

The amount of supplement ingested by the mother during the reproductive cycle was calculated as the total intake during the entire lactation period plus intake during the third trimester of pregnancy. Tertiles of intake were created (T1: 0–192.6 MJ; T2: 192.6–447.9 MJ, and T3: > 447.9 MJ). The 2 tertiles of highest intake did not differ significantly from each other in any analysis described below; therefore, these data were collapsed into one group (high-supplement group), which was contrasted with data from the lowest tertile (low-supplement group). For many women, the study team did not become aware of a new pregnancy during the first or sometimes part of the second trimester, so intake of the supplement during this period was not recorded reliably. Supplement intake by nonpregnant, nonlactating women was not recorded. Hence, our estimate of total supplement intake may have been underestimated, but relative intakes should be accurate because of consistent patterns of supplement consumption. We did not account for any supplement ingested by the infants, which was offered to them after 3 mo of age. Actually, infants of high-supplement mothers had higher supplement intakes than infants of low-supplement mothers and therefore depended less on breast milk and home diet for their nutrients (18). Thus, high-supplement mothers benefited from both increased supplement intake and lower breast-feeding demands. In summary, our comparison of high- and low-supplement mothers should be valid when comparing mothers with different initial energy balances.

In our sample, women consuming atole ingested more energy and protein from the supplement than did women ingesting fresco and their $\Delta W$ and $\Delta BW$ values were higher. However, for the same energy intake the effects were the same for both supplements, as expected from the lack of a protein effect in the overall study. Also, interaction terms for type of supplement in the regression models were nonsignificant.

Sample selection

Ethical approval for these secondary data analyses was granted by the University Committee on Human Subjects at Cornell University. Anthropometric measurements in mothers were included in the INCAP study in 1971. Between January 1971 and February 1977, 1016 live-born singleton births were recorded within the INCAP study (Figure 1); of these infants, 135 had no siblings born into the study. The remaining sibling pairs formed the basis for the current analysis, contributing information on 485 complete reproductive cycles. Complete data were available on $\Delta W$ and $\Delta BW$ for 283 of these 485 reproductive cycles. Of these 283 reproductive cycles, data on length of gestation and supplementary intake were available for 180
In malnourished and marginally nourished women, a priori hypotheses:

1. In malnourished and marginally nourished women, \( \Delta W \) is negatively and \( \Delta BW \) is positively, linearly related to initial maternal weight.

2. In malnourished and marginally nourished women, there is an interaction between level of maternal supplement intake and initial maternal weight, with respect to their effects on \( \Delta W \) and \( \Delta BW \). Hence, a maternal supplement will primarily prevent a negative \( \Delta BW \) in malnourished women but a negative \( \Delta W \) in marginally nourished women.

3. In well-nourished women, \( \Delta W \) and \( \Delta BW \) are not associated with initial maternal weight.

4. In well-nourished women, there is no interaction between level of maternal supplement intake and initial maternal weight with respect to their effects on \( \Delta W \) and \( \Delta BW \).

On the basis of the Guatemalan data as well as on experiences from the studies on Pakistani (8) and Indonesian (9) populations, an initial weight of 50 kg was used as a meaningful cutoff point between marginally and well-nourished women. Hence, we refer to our Guatemalan subjects with an initial weight \( \geq 50 \) kg as having normal weight (representing well-nourished women) and women with an initial weight < 50 kg as having low weight (representing marginally nourished women). On the basis of the results from our linear regression models, women at the lowest end of the distribution of initial weights were considered to have very-low weight (representing malnourished women). The whole group of women weighing < 50 kg had a mean height below the 5th percentile of the Canadian standards (19). Thus, their relatively normal body mass index of \( \approx 20 \) reflected a large height deficit masking their weight deficit. Other indications that these women were not well-nourished were mean triceps-skinfold-thickness values below the 5th percentile of the National Center for Health Statistics standards (19) and a mean birth weight of their infants of 2.9 kg. For women with an initial weight < 50 kg, the following 2 models were fitted with indicator variables for amount of supplement:

\[
\Delta W = b_0 + b_1 (\text{initial maternal weight}) + b_2Z_1 + \ldots + b_pZ_p \\
\Delta BW = b_0 + b_1 (\text{initial maternal weight}) + b_2Z_1 + \ldots + b_pZ_p
\]

where \( Z \) represents potential confounding variables [length of reproductive cycle, sex of both siblings, birth weight of first infant, and a dummy variable for parity (1, 2–9, and > 9)]. These variables were selected on the basis of knowledge of the literature and were evaluated by investigating their relation to the outcome variables as well as to their effect on other covariates in the models. No women smoked and there was no effect of season of measurement on maternal weight. Between 1971 and 1977, maternal mean weight did not increase although the proportion of mothers with a weight < 45 kg decreased from 36.8% to 29.6%.

Our assumption of a linear model was valid, as indicated by nonsignificant squared terms of both initial maternal weight and length of reproductive cycle. Similar models were fitted for well-nourished women. Also, nonlinear relations were nonsignificant. Analyses based on body mass index and thigh-skinfold thickness rather than weight were carried out as well. These results did not differ significantly from those based on weight, and, because changes in weight are easier to visualize than changes in body mass index or thigh-skinfold thickness, results based on weight are presented below.

All statistical analyses were done by using Statistical Analysis System software (version 5; SAS Institute Inc, Cary, NC) and the Statistical Package for Social Sciences (version 6.0: SPSS Inc, Chicago). Differences in basic characteristics among the

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**FIGURE 1.** Sample selection procedure for the Institute of Nutrition of Central America and Panama (INCAP) study (1971–1977). \( \Delta W \), overall maternal weight change; \( \Delta BW \), difference in birth weight between first and second (study) child.
groups were evaluated by using one-way ANOVA (α = 0.05, two-tailed). Significance of the slopes as well as the interaction terms were investigated by using Student’s t test (α = 0.05 for slopes and α = 0.10 for interaction terms); these were one-tailed because of a priori expectations based on our previous research.

RESULTS

As shown in Table 1, basic characteristics of the women with an initial weight < 50 kg (low weight) as well as the women with an initial weight ≥ 50 kg (normal weight) are shown according to low or high supplement intake. As expected from the classification scheme, the low-weight women had a significantly lower initial weight, height, body mass index, and birth weight of first infant than the normal-weight women. Normal-weight women ingesting the high supplement had a significantly greater parity and age than women in the other 3 groups. The reproductive cycle was shortest in normal-weight women ingesting the low supplement. The proportion of male and female newborns was similar for all 4 groups for both siblings (data not shown). Also as expected from the classification scheme, women in the high-supplement group ingested significantly more supplement than did women in the low-supplement group.

Relations between initial maternal weight and both ΔW and ΔBW at the 2 supplement intakes are illustrated for women with initial weight < 50 kg in Figures 2 and 3. Those in the low-supplement group had a significant decrease in ΔW with higher initial maternal weight (Figure 2; P = 0.04). Low-weight women experienced a net loss of ≈1 kg during the reproductive cycle. Concurrently, for these women there was a significant increase in ΔBW with higher initial maternal weight (Figure 3; P = 0.009). Very-low-weight women thus experienced a negative trend in infant birth weight of ≈500 g between 2 consecutive deliveries; in contrast, low-weight women had infants with similar birth weights in their 2 consecutive deliveries.

For women ingesting the high supplement, there was almost no change in ΔW with increasing initial maternal weight (negative slope, P = 0.42) nor in ΔBW (positive slope, P = 0.30). The fact that the relations between initial maternal weight and ΔW and ΔBW were significantly different for the 2 supplement groups was confirmed by significant interaction terms between level of supplement intake and initial maternal weight in the 2 models (P = 0.09 for ΔW, Table 2; P = 0.04 for ΔBW, Table 3).

For normal-weight women (data not shown), both the low- and high-supplement groups had a weak negative relation between initial maternal weight and ΔW (P = 0.42 and 0.50, respectively) as well as a weak positive relation between initial maternal weight and ΔBW (P = 0.29 and 0.13, respectively). Thus, as expected, initial maternal weight had little effect on ΔW and ΔBW in normal-weight women nor did level of supplement intake.

DISCUSSION

Validity of the results

Many women were excluded from the analyses because of missing information (Figure 1). However, in comparisons of women included and excluded, no significant differences were found for any of the basic characteristics, except for age. Analyses also were performed on the 103 women for whom information on gestational age, supplement intake, or both was missing. In these analyses, gestational age was set to a constant (the mean for the sample) and the portion of total supplementary intake that was missing was set to 0. This group did not differ significantly from the 176 women described here in their relations between initial weight and ΔW and ΔBW, as indicated by nonsignificant interaction terms in analyses including both groups of women. Thus, the

TABLE 1

Basic characteristics of the Guatemalan women by initial weight and amount of supplement ingested

<table>
<thead>
<tr>
<th></th>
<th>Malnourished and marginally nourished women</th>
<th>Well-nourished women</th>
</tr>
</thead>
<tbody>
<tr>
<td>(initial weight &lt;50 kg)</td>
<td>(initial weight ≥50 kg)</td>
<td></td>
</tr>
<tr>
<td>Low supplement</td>
<td>High supplement</td>
<td>Low supplement</td>
</tr>
<tr>
<td>(n = 56)</td>
<td>(n = 83)</td>
<td>(n = 23)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>44.7 ± 3.2†</td>
<td>44.8 ± 3.2†</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>147.7 ± 4.4†</td>
<td>148.0 ± 5.4†</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>20.5 ± 1.1†</td>
<td>20.5 ± 1.8†</td>
</tr>
<tr>
<td>Parity</td>
<td>2.8 ± 2.6†</td>
<td>2.4 ± 2.1†</td>
</tr>
<tr>
<td>Age (y)</td>
<td>25.6 ± 7.2†</td>
<td>25.2 ± 5.4†</td>
</tr>
<tr>
<td>Length of reproductive cycle (d)</td>
<td>721 ± 226a</td>
<td>747 ± 144a</td>
</tr>
<tr>
<td>Supplement intake (MJ)</td>
<td>108.6 ± 60.8a</td>
<td>457.6 ± 228.8b</td>
</tr>
<tr>
<td>Birth weight of first infant (kg)</td>
<td>2.90 ± 0.39a</td>
<td>2.92 ± 0.39a</td>
</tr>
</tbody>
</table>

† X ± SD. Means in the same row with different superscript letters are significantly different, P < 0.05 (ANOVA and pairwise t test).

1 Adjusted for length of reproductive cycle: initial maternal weight < 50 kg (n = 119); model F = 2.042, P = 0.093.
2 One-sided test.
3 High = 0, low = 1.
176 women with the most complete information did not differ significantly from the other women. There are no apparent ways that self-selection could have produced these results, except for length of reproductive cycle (see Sample selection). Therefore, we evaluated length of reproductive cycle as a potential confounding factor in all models and found no effect. However, inferences should not be extended to women with lower fertility, longer reproductive cycles, or both without caution.

**Partitioning of resources between mother and offspring under scarce conditions**

Our results confirm our earlier findings in animals and humans that, under conditions of scarcity, resources are partitioned differently between mothers and their infants, depending on the mothers’ initial nutritional status. Indeed, maternal depletion occurs in women well-nourished enough to provide for their offspring but unable to prevent a negative energy balance of their own. Ultimately, this depletion has a lower limit at which it ceases and the birth weight of the offspring is affected instead.

When presenting our framework (7), we suggested that self-selection could have produced these results, except for length of reproductive cycle (see Sample selection). Therefore, we evaluated length of reproductive cycle as a potential confounding factor in all models and found no effect. However, inferences should not be extended to women with lower fertility, longer reproductive cycles, or both without caution.

**TABLE 3**
Multiple linear regression coefficients for differences in birth weight between 2 consecutive newborns (ΔBW) as predicted by maternal supplement intake and initial weight

<table>
<thead>
<tr>
<th></th>
<th>β</th>
<th>SE</th>
<th>P²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>0.052</td>
<td>0.076</td>
<td>0.245</td>
</tr>
<tr>
<td>Supplement level</td>
<td>0.122</td>
<td>0.140</td>
<td>0.193</td>
</tr>
<tr>
<td>Maternal initial weight</td>
<td>0.008</td>
<td>0.016</td>
<td>0.300</td>
</tr>
<tr>
<td>Maternal initial weight × supplement</td>
<td>0.051</td>
<td>0.029</td>
<td>0.043</td>
</tr>
<tr>
<td>Length of reproductive cycle (d)</td>
<td>0.00007</td>
<td>0.0002</td>
<td>0.381</td>
</tr>
</tbody>
</table>

¹Adjusted for length of reproductive cycle; initial maternal weight < 50 kg (n = 119); model F = 1.716, P = 0.151.
²One-sided test.
³High = 0, low = 1.

The concurrent negative effects on the offspring suggest a preferential partitioning of nutrients to the mother in the very-low-weight, unsupplemented women, which protects the mother at the expense of her fetus. The true long-term cost of these adaptations to the mother-infant dyad and their community are unknown. However, the concept of maternal depletion must be expanded to address those situations in which mothers replete themselves at the expense of their offspring.

**Benefits of a nutritional supplement provided to pregnant and lactating women**

Our results indicate that a nutritional supplement provided to the mother may benefit her infant (ie, prevent an otherwise negative trend in birth weight from one sibling to the next) if the mother is malnourished (our very-low-weight subjects), and it may benefit the mothers (ie, prevent an otherwise negative trend in maternal weight over a reproductive cycle) if provided to marginally nourished mothers (our low-weight subjects). The supplement had no effect on either overall maternal weight change or trends in infant birth weight across a reproductive cycle in well-nourished women (our normal-weight subjects), which are likely to be adequate without supplementation.

As mentioned earlier, reviews of nutritional supplementation studies have concluded that supplements have little benefit to either mother or infant (3, 4). However, neither of these reviews evaluated benefits over an entire reproductive cycle and thus could not detect the full benefit to the mothers and their infants. More importantly, these evaluations were not done at different levels of malnutrition and therefore the differential effects of supplementation at these different levels may have hid the true responses. Thus, the fact that mothers and infants benefited differently and that the responses were opposite at different levels of maternal malnutrition were not identified.
In conclusion, our results showed that both mothers and their infants benefited when a nutritional supplement was provided to the mother. The dynamic nature of these benefits within the mother-infant dyad were probably detected because a full reproductive cycle was investigated and both infants and mothers were evaluated according to initial maternal nutritional status. This finding is important to policymakers and program planners, so that nutrition interventions that benefit both mother and infant can be properly designed and evaluated.

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REFERENCES