Nutritional Supplementation During Two Consecutive Pregnancies and the Interim Lactation Period: Effect on Birth Weight

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ABSTRACT. The study consisted of 169 mothers enrolled during two consecutive pregnancies and the intervening lactation period in the Guatemalan Nutritional Supplementation Study. Women were grouped for this analysis according to the levels of caloric supplementation that they received (high or low) during two consecutive pregnancies and the period between them. The supplement also contained minerals and vitamins. Data were analyzed adjusting for maternal height, birth interval, parity, length of lactation, socioeconomic status, birth weight of the first offspring, gestational age of the second offspring, and caloric supplementation, expressed either in continuous fashion (total intake) or as caloric supplementation per week. The adjusted mean birth weights of the second offspring of women with high supplementation during two pregnancies (about an extra 180 kcal/d), and the in-between lactation period (about an extra 245 kcal/d), were up to 301 g greater than that of the low supplementation group. Women with high supplementation while breast-feeding their first offsprings and during their second pregnancies had babies up to 150 g heavier than the reference group; those mothers with high supplementation only during the second pregnancy had infants about 124 g heavier than those of the low supplementation group. Therefore, high supplementation during two consecutive pregnancies and their intervening lactation period among chronically, yet moderately, malnourished women was capable of increasing the mean birth weight to levels closer to those reported for industrialized populations. The mean birth weight increase is between two and three times greater than the effect shown in almost all of the previous studies of this topic. *Pediatrics* 1988;81:51-57; *nutritional supplementation, pregnancy, lactation, birth weight.*

Nutritional supplementation during pregnancy has been the subject of multidisciplinary research for decades. The interest in improving the nutritional status of pregnant women derives from the strong epidemiologic evidence of the relationship between maternal nutritional status and birth weight.

Based on this evidence, intervention studies have been conducted with human populations in developed and developing countries, offering various food supplements containing different quantities of nutrients and using both noncontrolled and controlled study designs. Data analyses were either simple and straightforward or sophisticated.[1,2]

Surprisingly, and regardless of methodologic and practical differences, the effect of nutritional supplementation during one pregnancy on birth weight has consistently been modest, with an average increase of less than 100 g.[1] Yet, this limited impact was to be expected, given the characteristics of the populations studied. For instance, most research projects were conducted in developing countries, where moderate, yet chronic, malnutrition is widespread among poor women.[3,4] Thus, it was unrealistic to expect that this handicap developed during many generations could be overcome in a period of 3 to 5 months of modest nutritional supplementation and initiated only after the onset of pregnancy. However, if chronically and moderately malnourished women are supplemented during two consecutive pregnancies and the intervening lactation period, there is a greater and biologically more significant improvement in infant birth weight than previously reported.

MATERIALS AND METHODS

The study population consisted of 169 mothers and their offspring enrolled during two consecutive pregnancies and the interim lactation period in the Guatemalan Longitudinal Study of Nutritional

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Supplementation, Growth, and Development, conducted by the Institute of Nutrition of Central America and Panama (INCAP), in four rural communities in Guatemala between January 1969 and February 1977. This population has been described extensively elsewhere.[5] All infants studied were single births and had no cogenital malformations. Nurses provided antenatal care to all mothers during the study period.

Two types of supplements were offered to pregnancy and/or lactating women and children: (1) a high-protein/high-calorie drink called *atole* (a warm gruel-like beverage) was provided in two villages and (2) a no-protein/low-calorie cold liquid drink called *fresco* (similar to Kool-Aid) was provided in the other two villages. The supplements also contained vitamins and minerals. Mothers and children voluntarily consumed the supplements at the distribution centers, and the quantities ingested daily were carefully recorded.

Additional information included home dietary intakes using a 24-hour recall method, maternal and newborn anthropometric measures, maternal age, morbidity, birth order, birth interval, and socioeconomic status. Birth weight was obtained by trained personnel using carefully standardized procedures and calibrated scales. None of the women smoked, therefore, no adjustment is made for this variable.

The effect of maternal supplementation on birth weight of the second offspring was analyzed with the independent variable expressed as caloric intake per week of gestation and as total caloric intake. The study population was divided for these analyses into four groups based on the quantity of supplemented calories voluntarily consumed by the mother during two consecutive pregnancies and the period between gestations. Therefore, the groups formed are the result of the level of participation in the study and not a random allocation of patients.

A high-high-high group (HHH) ($n = 21$) was composed of women receiving >20,000 kcal during each pregnancy and >40,000 kcal during the interim period. Conversely, a low-low-low group (LLL) ($n = 50$) had supplementation of ≤20,000 kcal during each pregnancy and ≤40,000 kcal during the period between gestations.

All other possible combinations of supplementation during each pregnancy and the intergestational period were evaluated using the same cutoff points. From them, two additional groups emerged: a low-high-high (LHH) ($n = 55$) supplemented group, whose members had low caloric supplementation during the first pregnancy but high supplementation during lactation and the second gestation and a low-low-high (LLH) ($n = 27$), whose members had high supplementation only during the last pregnancy. This last group represents the case of almost all previous studies of nutritional supplementation during pregnancy. There were only 16 women enrolled in the study with supplementation levels corresponding to the other possible group combinations; thus, there were few women for all other groups, and they were excluded from this analysis.

The cutoff point used during pregnancy (≤20,000 kcal) was based on previous reports from this population[6,7]; the cutoff point for lactation (≤40,000 kcal) was equivalent to the supplementation of two pregnancies and was chosen because the mean lactation period was between 16 and 18 months in this population.

Given that the length of the intergestational period and, to a lesser degree, the duration of gestations varied among women, the four supplementation groups were also defined in terms of caloric intake per week. The cutoff point between high and low intake was 500 kcal/wk for the three periods. This was equivalent to the cutoff points used for absolute caloric intakes. The principal outcome variable of the study is the birth weight (in grams) of the second offspring.

Analysis of variance was used to compare the crude birth weights and to evaluate trends among groups. Multiple regression models with indicator variables for the supplementation groups[8] were used to analyze the differences in birth weight among the supplementation groups after controlling for several potential confounding factors (adjusted birth weight). These models can be illustrated as four different regression lines (one for each supplementation group) with either a common or a different slope, depending on the statistical significance of the interaction terms. If no statistically significant interactions are present (common slope), the regression coefficients for each group represent the birth weight difference between the supplemented group and the LLL group. This model allowed comparisons among birth weight means, adjusting for several possible covariates, and permits testing for interactions.

A multiple linear regression analysis was also performed, using the total quantity of calories received from supplementation during both pregnancies and the lactation period expressed as a continuous variable.

All analyses used one-sided P values because of an a priori hypothesis of a positive association between supplement intake and birth weight.

RESULTS

Descriptive statistics for the studied variables in

TABLE 1. Descriptive Statistics for Studied Variables in Four Supplemented Groups

Variable	High-High-High n	Mean	SD	Low-High-High n	Mean	SD	Low-Low-High n	Mean	SD	Low-Low-Low n	Mean	SD
Mother's age (yr)	21	29.8	6.0	55	28.0	7.0	27	27.4	6.5	50	28.2	6.6
Parity	21	4.7	2.5	55	4.4	3.3	27	3.5	2.3	50	4.0	3.0
Mother's height (cm)	21	150.9	5.1	55	148.9	5.1	27	148.7	6.4	50	148.7	4.4
Socioeconomic index	21	−23.1	97.3	51	−17.3	87.5	27	−32.5	107.6	49	4.1	71.8
Birth interval (mo)	21	24.2	5.1	55	25.0	4.7	27	25.7	5.1	50	24.5	4.8
Length of lactation (mo)	21	17.2	4.1	54	17.1	5.2	24	16.0	5.0	42	15.9	5.6
Birth wt of first infant (g)	14	3,379.0	515.0*	27	2,855.6	471.0	11	3,073.0	429.0	26	2,969.0	424.0
Gestational age (wk)												
1st pregnancy	20	39.8	2.5	34	39.9	2.0	13	38.9	2.6	28	38.6	2.5
2nd pregnancy	19	39.4	2.3	50	40.0	2.1	27	39.5	2.4	45	38.8	2.9
Supplementation (1,000 kcal)												
1st pregnancy	21	43	27	55	6	6	27	5	6	50	2	3
Lactation	21	150	108	55	110	62	27	14	10	50	11	12
2nd pregnancy	21	62	25	55	46	20	27	36	14	50	6	7

Supplementation Groups (1st Pregnancy-Lactation-2nd Pregnancy)

* $P < .01$ from all other groups.

TABLE 2. Crude and Adjusted Birth Weight of Second Offspring for Four Supplementation Groups: Level of Supplementation as Total Caloric Intake*

Supplementation Group (1st Pregnancy-Lactation-2nd Pregnancy)	Unadjusted Analysis n	Mean (g)	SD	Adjusted Analysis (Mean Differences From LLL Group): Parity, Maternal Height — Mean	SE	Parity, Maternal Height, and Gestational Age 2nd Pregnancy — Mean	SE	Parity, Maternal Height, and Birth Wt 1st Infant — Mean	SE
High-high-high	21	3,290†	514	301†,§	123	267†,§	123	246†,§	157
Low-high-high	55	3,105	474	150‡	91	113‡	94	193‡	123
Low-low-high	27	3,056	378	124	112	100	112	202	163
Low-low-low	50	2,944	501						

* High, high supplementation >20,000 kcal pregnancy, >40,000 kcal lactation; Low, low supplementation ≤20,000 kcal pregnancy, ≤40,000 kcal lactation.
† $P < .05$ (test for linear trend).
‡ $P < .05$; one-tailed.
§ $P < .025$ compared with LLL group.

the four supplementation groups are presented in Table 1. There were no significant differences in birth intervals (mean range 24.2 to 25 months), length of lactation (mean range 15.9 to 17.2 months), mother's age (mean range 27.4 to 29.8 years), maternal height (mean range 148.7 to 150.9 cm), and parity (mean range 3.5 to 4.7 pregnancies) (Table 1). The LLL group had a gestational age of 38.8 weeks, about 1 week shorter than the other groups (*P* value not significant). In contrast, the same group (LLL) had a higher mean socioeconomic status index, although not statistically significant than the other three groups; whereas the HHH and LLH groups were economically the poorest (Table 1).

Mean birth weights of the first infants are also presented in Table 1. The HHH group had a higher mean birth weight (3,379 ± 515 g) ($P < .01$) than the other groups. Among the three groups with low caloric supplementation during the first pregnancy, the mean birth weights were similar and not statistically significant.

Descriptive statistics were also compared for (1) the population studied here (supplemented during two pregnancies), (2) women in the Guatemalan Longitudinal Study supplemented during one single pregnancy, and (3) the total pregnant population of the longitudinal study. These groups had similar sociodemographic and maternal characteristics.

The effect of total caloric supplementation during pregnancies and lactation on the birth weight of the second offspring are shown in Table 2. The HHH group had the highest crude and adjusted birth weights, whereas the LLL group had the lowest. There was a statistically significant linear trend ($P < .05$) of birth weight from the highest

(HHH) to the lowest (LLL) supplemented group in both crude and adjusted means. The HHH group had a mean birth weight adjusted for maternal height and parity 301 g greater than the LLL group ($P < .025$); the LHH group was 150 g heavier than the LLL group when adjusted ($P < .05$). Mothers with high supplementation only during the last pregnancy had newborns 124 g heavier than the LLL group when adjusted (P value not significant) (Table 2).

Length of gestation of the second pregnancy was introduced into the model, along with the mother's height and parity. After controlling for these covariates, the difference in birth weight between the HHH (n = 19) and the LLL groups (n = 44) was 267 g ($P < .025$). The difference between the LLL and the LHH groups (n = 53) was 113 ($P < .05$) and between the former and the LLH group (n = 27) was 100 g (P value not significant) (Table 2).

The effect of caloric supplementation adjusted for the birth weight of the first offspring was also evaluated. The sample size decreased to 79. The adjusted difference in the birth weight of the second pregnancy between the LLL group (n = 26) and the HHH group (n = 14) was 246 g ($P < .025$). The difference between the LLL and the LHH group (n = 23) was 193 g ($P < .05$) and between the LLL and the LLH group (n = 11) was 202 g (P value not significant) (Table 2). There was a statistically significant ($P <.05$) linear trend of birth weight difference from the highest to the lowest supplemented groups in all adjusted mean values (Table 2).

Supplementation during pregnancies and lactation was then expressed as intake per week. Four supplementation groups were constructed as described before. The sample size was reduced to 97 because this analysis required information about gestational age of two pregnancies and length of lactation for all participants. There were no significant differences among the groups with respect to mother's age, parity, maternal height, birth interval, or length of lactation. The LLL and LLH groups had reduced gestational ages (39.1 ± 2.38 and 38.1 ± 3.36 weeks, respectively) relative to the other two groups (39.8 ± 2.73 and 39.6 ± 2.57 weeks, respectively). The LLL group had a higher but nonsignificant mean socioeconomic status index than the other three groups, with the HHH group having the lowest. Finally, the mean birth weight of the first offspring in the HHH group was higher (3,333 ± 481 g) ($P < .01$) than in the other groups. Again, the three groups with low caloric intake during the first gestation had similar birth weights during that pregnancy. The effect of supplementation, expressed in kilocalories per week, on birth weight for the four groups is presented in Table 3. There was a statistically significant trend ($P < .01$) from the HHH group (3,257 ± 530 g) to the LLL group (2,960 ± 328 g). Parity and maternal height, the only two significant variables in the last model, were adjusted for and the HHH group had a mean birth weight 238 g higher than the LLL group ($P < .02$). The LHH and LLH groups had birth weights 123 g and 113 g, respectively, higher than the LLL group (P value not significant) (Table 3). Unfortunately, no data can be presented for which the birth weight of the first offspring was adjusted for because adding this variable into this analysis reduced sample size to an unacceptable level.

The same pattern of birth weight differences was thus observed in the crude and adjusted analysis when the independent variable was expressed as either total supplementation or supplementation per week of gestation or lactation (Tables 2 and 3).

The effect of supplementation on birth weight of the second offspring was also explored in a multiple linear regression model using as independent variables the total calories received during both pregnancies and lactation, maternal height, parity, birth interval, length of lactation, gestational age of second offspring, and socioeconomic status of the fam-

TABLE 3. Crude and Adjusted Birth Weight of Second Offspring for Four Supplementation Groups: Level of Supplementation as Caloric Intake per Week of Gestation or Lactation*

Supplementation Groups (1st Pregnancy-Lactation-2nd Pregnancy)	Crude			Adjusted for Parity and Maternal Height†	
	n	Mean (g)	SD	(Differences With Low-Low-Low Group) Mean (g)	SE
High-high-high	21	3,257	530	238‡	129
Low-high-high	36	3,100	516	123	113
Low-low-high	15	3,087	346	113	142
Low-low-low	25	2,960	328		

* Level of supplementation as caloric intake per week of gestation or lactation. High, high supplementation >500 kcal/wk; Low, low supplementation ≤500 kcal/wk.
† Only two significant variables in model.
‡ $P < .025$ (one-tailed) compared with LLL group.

TABLE 4. Regression Analysis of Effect of Total Supplementation During Two Consecutive Pregnancies and Interim Lactation Period on Birth Weight of Second Offspring

	Partial Regression Coefficient	SE	Adjusted Regression Coefficient
Model 1 (n = 166)			
Total supplementation (kcal)	.134*	.004	.17
Mother's height (cm)	.015†	.007	
Parity	.022‡	.012	
Gestational age of 2nd pregnancy (wk)	.049*	.013	
Model 2 (n = 95)			
Total supplementation (kcal)	.088‡	.05	.18
Birth wt 1st infant (g)	.392*	.096	

* $P < .001$.
† $P < .025$.
‡ $P < .05$.

ily (n = 169). Three women had more than 431,564 kcal of supplementation, or 425 kcal/d, greater than the rest of the population, and were not included in this analysis (n = 166).

The final regression models, including only independent variables that were statistically significant at the $P < .05$ level, are shown in Table 4. Total caloric supplementation as a continuous variable is positively and significantly associated with birth weight of the second infant, after controlling for all variables including type of supplementation (protein and calories or just calories). Maternal height, parity, and gestational age during the second pregnancy also remained significant in the final model. Moreover, this relationship was present after adjusting for gestational age of the second offspring (model 1) and birth weight of the first infant (model 2). Total caloric supplementation, maternal height, and parity explained 10% of birth weight variability; adding gestational age to the model, an increase of up to 17% was observed. Total supplementation and birth weight of the first offspring explained 18% of the birth weight variability (Table 4).

DISCUSSION

Several methodologic issues are important. Women admitted themselves to the clinic voluntarily. Two factors operate against this possible self-selection effect. Women receiving higher supplementation were consistently in the poorest and least educated segment of the population. Therefore, these findings were not the result of low risk women (higher economic status, better educated) improving the outcome of the HHH group. Second, the effect of supplementation was also seen after controlling for birth weight of the first infant, thus eliminating the previous low or high birth weight as a possible motivation for attending the clinic. Note that adjusting for birth weight of the first infant is a powerful means to control for other biologic and socioeconomic characteristics of the mother associated with fetal growth.

Infants from the three groups with low caloric supplementation during the first pregnancy had similar and not statistically significant different mean birth weights. This evidence, strongly suggests that birth weights of infants in the three groups with low supplementation were similar during the first gestation but different during the second. Therefore, although the self-selection effect cannot be eliminated, it does not appear to have influenced the results obtained.

The sociodemographic characteristics of the subsample selected here, requiring at least two pregnancies during the study period, were similar to those of the total population in the original study. Furthermore, when women receiving high supplementation only during the second pregnancy were considered (Tables 2 and 3), the magnitude of the effect of supplementation on birth weight was slightly more than 100 g, similar to the 111-g effect originally reported.[7]

Controlling for the effect of length of gestation of the second pregnancy by including it in the model (Table 2) or expressing the independent variable as caloric supplementation per week (Table 3) showed a birth weight pattern similar to that in the unadjusted analysis, although the supplementation effect was reduced for the HHH group to 267 and 238 g, respectively. This result could indicate that part of the effect is an artifact of duration of supplementation. In other words, the longer the gestational period, the higher the time at risk during which to receive supplementation rather than the reverse (cart *v* horse artifact).

Evidence from these data indicates a treatment effect of supplementation on gestation age. Delgado et al[9] showed that caloric supplementation during the first and second trimesters significantly affected length of gestation. Villar et al[10] reported risk of preterm deliveries twice as high for mothers in the low rather than high supplementation group, when the independent variable, caloric supplementation, was constructed as kilocalories per day of gestation. Thus, the reduction in the supplementation impact after adjusting for length of gestation should be seen as a consequence of eliminating one mechanism by which the intervention affects fetal weight.

There was evidence. although not statistically significant, suggesting that supplements containing more proteins had a positive effect on birth weight. Nevertheless, caloric supplementation remained statistically significant after controlling for the type of supplementation, confirming its independent and positive effect on birth weight.

Finally, the larger the volume of supplementation the more vitamins and minerals were ingested. Given that no volume effect was observed at the two levels of caloric supplementation (low and high), a birth weight effect of vitamins and minerals is unlikely.[7]

Therefore, it is unlikely that these results, obtained after an extensive adjustment process including birth weight of the first infant and gestational age of the second pregnancy are due to women's self-selection, higher socioeconomic status, type of supplement, or better previous nutritional status of the high supplementation group.

High supplementation during two consecutive pregnancies (about an extra 180 kcal/d) and the intervening lactation period (about an extra 245 kcal/d) among chronically moderately malnourished women could increase the group mean birth weight to levels closer to those reported for populations in industrialized countries.[11] This represents between 230 and 300 g increase in the high supplementation group, compared with the low supplementation group, a quantity up to three times higher than the effect shown in many previous reports,[1,2] except for the Gambia study during the wet season.[12] In this case, women in marked negative energy balance receiving 431 kcal/d of supplementation increased the mean birth weight by 224 g.

It is evident that women without overt malnutrition[1,13-15] or in positive energy balance (eg, Gambian women during the dry season)[12] obtain a limited benefit from nutritional supplementation during only one pregnancy. Chronically moderately malnourished mothers also supplemented only during the index pregnancy experienced a modest impact on birth weight of about 100 g.[1,2,7,13] However, when women are in a negative energy balance (acute malnutrition), food supplementation that helps them overcome this metabolic situation produces a biologically significant increase in birth weight of approximately 230 g.[12] Moreover, chronically moderately malnourished mothers will dramatically benefit from extra food if the amount of supplementation and the period of treatment are proportional to the magnitude of their nutritional deficits. The expectation of a dramatic recovery from generations of poverty and food scarcity in a short time (no longer than half of a pregnancy) was an overly optimistic proposition.

The magnitude of birth weight increase here is even more significant if the modest amount of supplementation ingested by these women is considered. It may be the extra, yet prolonged, intake during pregnancies and lactation, rather than large amounts of supplementation during short periods of a given gestation, that produces the fetal growth effect.

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