Effect of Food Supplementation During Pregnancy on Birthweight

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ABSTRACT. The high prevalence of low-birthweight (≤ 2,500 gm) babies in many poor communities is a major public health problem. Studies in humans in situations of acute starvation suggest an effect of maternal nutrition on birthweight, but less clear results appear under situations of moderate maternal malnutrition. We studied the effects of food supplementation during pregnancy on birthweight in four rural villages of Guatemala, in which two types of supplements were distributed: protein-caloric and caloric.

The caloric supplementation increased the total caloric intake during pregnancy. In both supplements, the amount of calories supplemented during pregnancy showed a consistent association with birthweight. In the combined sample the proportion of low-birthweight babies in the high-supplement group (≥ 20,000 supplemented calories during pregnancy) was 9% compared with 19% in the low-supplement group (< 20,000 supplemented calories during pregnancy). The relationship between caloric supplementation and birthweight (29 gm of birthweight per 10,000 supplemented calories) was basically unchanged after controlling for the maternal home diet, height, head circumference, parity, gestational age, duration of disease during pregnancy, socioeconomic status, and different rates of missing data. Moreover, a similar association was found in consecutive pregnancies of the same mother. We concluded that caloric supplementation during pregnancy produced the observed increase in birthweight. *Pediatrics*, 56:508-520, 1975, LOW BIRTHWEIGHT, FOOD SUPPLEMENTATION, PREGNANCY, NUTRITION.

The proportion of babies with low birthweight (≤ 2,500 gm) ranges between 13% and 43% in the low socioeconomic strata of many countries, including some developed nations.[1] These babies are less likely to survive during the first year of life than babies with higher birthweights.[2,3] This human wastage places considerable stress on poor societies, both emotionally and economically. Moreover, those low-birthweight babies who do survive frequently rank low on tests of mental development,[4-6] suggesting less ability to function economically and socially in a modern society. For these reasons, the high prevalence of LBW babies is a major public health problem and may also be a serious obstacle to national development.

Maternal malnutrition has been implicated as one of several environmental factors contributing to low birthweight. This paper briefly reviews the extant literature on the relationship between maternal nutrition and birthweight and presents the final results of a four-year experiment in which food supplements were provided to pregnant women in four rural villages in Guatemala.

LITERATURE REVIEW

Experiments with animals have shown that severe caloric or protein malnutrition during pregnancy delays fetal growth[7] and that this growth retardation may be irreversible in those

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organs in which the nutritional insult has affected the rate of cell division.[8]

In humans, under conditions of acute starvation, a relationship between maternal nutrition and birthweight has been reported. Babies born from pregnancies occurring during periods of famine had consistently lower birthweights than babies born during times of adequate food availability in the same country.[9-11]

On the other hand, the impact of moderate levels of malnutrition on fetal growth is less clear. The consistent association between birthweight and maternal weight before pregnancy and/or weight gain during pregnancy has been interpreted by some as evidence for a nutritional effect on birthweight.[1,12] However, studies using information from dietary surveys or food supplementation programs have reported contradictory results. While in some studies an association between maternal food intake and birthweight was evident,[13,14] others have failed to reveal such association.[15-17]

The absence of a clear relationship between birthweight and food intake during pregnancy could be due in part to the fact that most of the women of the studied populations were relatively well nourished.[15-17] On the other hand, those studies showing an association between maternal nutrient intake and birthweight[13,14] are themselves inconclusive because the influence of potentially confounding variables such as infectious disease was not explicitly investigated.[18]

An analogous objection holds for our previous findings indicating that among pregnant women from rural Guatemala the average birthweight increased progressively as home dietary intake increased.[19] Although this relationship remained after the weight of the newborns was corrected for important maternal characteristics, we were unable to completely discard the possibility that nonnutritional factors could have produced both greater maternal food intake and higher birthweight.

Similarly, the results of Iyengar's experiment in India,[20] suggesting a strong effect of maternal food supplementation on birthweight, are difficult to interpret since, in order to implement the food supplementation program, the mothers in the experimental group were hospitalized during the last six to eight weeks of gestation. Hospitalization could have resulted in decreased rates of infection and reduced physical activity and these factors, in turn, may have been responsible for the observed increase in birthweight.[21,22]

In conclusion, there are two serious difficulties to be faced in studying the effect of moderate maternal malnutrition on birthweight: (1) the precise quantification of maternal nutritional status and (2) the control of confounding factors in order to be able to infer that the detected association is not artifactual.

Although pregnant women may adapt to widely varying nutrient intake without affecting the weight of the newborn, it is also possible that there are minimum nutrient requirements which must be satisfied to maintain optimal rates of fetal growth. Thus, the probability of finding a relationship between maternal nutrition during pregnancy and birthweight should be greater if this hypothesis is tested through a nutritional intervention program focused on malnourished mothers.

The present article reports the results of an experiment in which a nutritional supplement was made available to a chronically malnourished population of women of child-bearing age. Important maternal variables, capable of obscuring a relationship between maternal nutrition and birthweight, were also investigated.

TABLE I

EXPERIMENTAL DESIGN FOR FOUR VILLAGES*

Information†	*When Collected*
Obstetrical history	Once
Clinical examination	Quarterly
Anthropometry	Quarterly
Surveys	
Diet	Quarterly
Morbidity	Fortnightly
Attendance at feeding center	Daily
Amount of supplement ingested	Daily
Socioeconomic status	Estimated
Birthweight	At delivery

*Two villages received *atole*, a protein-calorie supplement, and two *fresco*, a caloric supplement.

†Pregnancy was diagnosed by absence of menstruation; these surveys were made fortnightly.

METHODS

Experimental Design

The data presented here are drawn from a long-term prospective study of the effects of chronic malnutrition on physical growth and mental development.[23] The experimental design and the principal examinations made during the prenatal period and at birth are presented in Table 1. Two types of food supplements were provided: *atole* (a gruel) and *fresco* (a refreshing, cool drink). Two villages received *atole* while the other two received *fresco*. Attendance at the supplementation center was voluntary and this resulted in a

TABLE II

NUTRIENT CONTENT PER CUP*

Nutrient	Type of Supplement	
	Atole	*Fresco*
Total calories (kcal)	163	59
Protein (gm)	11	—
Fats (gm)	0.7	—
Carbohydrates (gm)	27	15.3
Ascorbic acid (mg)	4.0	4.0
Calcium (gm)	0.4	—
Phosphorus (gm)	0.3	—
Thiamine (mg)	1.1	1.1
Riboflavin (mg)	1.5	1.5
Niacin (mg)	18.5	18.5
Vitamin A (mg)	1.2	1.2
Iron (mg)	5.4	5.0
Fluor (mg)	0.2	0.2

*Figures rounded to the nearest tenth. One cup = 180 ml.

wide range of supplement intake during pregnancy. In addition, all villagers received preventive and curative medical care.

Table II presents the nutrient content for both *atole* and *fresco*. It should be stressed that the *fresco* contains no protein and provides only one third of the calories contained in an equal volume of *atole*. In addition, both preparations contain similar concentrations of the vitamins and minerals which are possibly limiting in the diets of this population.

Description of the Population

The median family income in the four villages is approximately $200 per year. The typical house is built of adobe and has no sanitary facilities. Drinking water is grossly contaminated. Before the study began around 15% of the newborns died during the first year of life, a very high figure when compared with the current rates of less than 2% in developed societies. Clinically severe malnutrition (kwashiorkor) was prevalent, and children were severely retarded in physical growth at 7 years of age.[21-25] Intrauterine infections were also very common as compared with developed societies.[26] Corn and beans are the principal components of the home diet, with animal protein forming 12% of the total protein intake. Dietary surveys indicate that the average daily dietary intake throughout pregnancy was about 1,500 calories and 40 gm of protein. At the time the study began, malnutrition and infectious diseases were endemic in the four villages.

The average maternal height was 149 cm; the mean maternal weight at the end of the first trimester of pregnancy was 49 kg and the mean weight gain during gestation was 7 kg, about one half the norms.[27] The median number of previous deliveries was four (range, 0 to 13) and the median of age was 26 years (range, 14 to 46 years). In a small sample of newborns (No. = 42) collected at the beginning of this study, the average birthweight was 3,000 gm and one third of the newborns with normal gestational ages (No. = 39) weighed 2,500 gm or less. Although data are not available from similar villages, it should be noted that 41% of the newborns weighed 2,500 gm or less in one Mayan Indian rural village in which there was no nutritional intervention.[3]

Variables Selected for the Present Analysis

The six groups of variables to be analyzed in the present article are shown in Table III. Data collection on these variables was standardized and the data collectors were systematically rotated among the four study villages.

Maternal ingestion of food during pregnancy included two variables: ingestion of the supplement (the experimental treatment) and estimates of daily home diet intake for the last two trimesters of pregnancy. Maternal home intake was estimated through 24- and 72-hour recall surveys at the end of each trimester of pregnancy. Previous analyses have shown that the home diet intake during the first trimester of pregnancy was significantly lower than the intake during the last two trimesters and that there was no significant difference between the 24-hour and 72-hour recall surveys.[19] Both variables, supplement and home diet intake, were expressed in terms of calories because preliminary analyses made during the last four years have shown that caloric intake during pregnancy was consistently associated with birthweight in this population.[28,29]

Maternal anthropometric examinations included height and head circumference as well as weight at the end of the first trimester of pregnancy. First-trimester weight may be considered an indicator of maternal nutritional status at the beginning of pregnancy while height and head circumference probably reflect maternal physical growth during infancy and childhood. Previous analyses in this population have shown that the differences in head circumference and height between the adult women of this population and United States standards were 3.9 and 16.9 cm, respectively. The differences observed for head circumference at 2 years of age and for height at 7 years of age between the girls of this population and those of the same United States standards were 3.0 and 12.1 cm, respectively. These results suggest, therefore, that retardation in maternal height and head circumference reflects physical growth retardation in early life.[1]

The obstetrical variables were parity, expressed as the number of previous births, and gestational age which is elapsed time in weeks from conception to birth. Parity was determined by interviewing the mother and reviewing the village civil registry. Onset of pregnancy dated from the absence of a menstrual period. Since all mothers with preschool children were visited every two weeks, this information was elicited within 15 days of the missed period. Primiparas and those women with postpartum amenorrhea who became pregnant were usually identified somewhat later. In addition to these variables, birth interval since the previous baby, age of the mother, and duration of lactation during the present pregnancy were also recorded.

Maternal morbidity during pregnancy was estimated through the same fortnightly interviews used to monitor menstruation. A composite morbidity indicator was generated by adding the number of days per month of pregnancy during which the mother was ill with diarrhea, anorexia, or remained in bed due to illness. In previous analyses, these components were shown to be significantly associated with birthweight. Lastly, the risk of intrauterine infection was estimated by measuring IgM levels in cord blood.[28]

The socioeconomic status of the family was described by a composite scale reflecting the physical conditions of the house, the mother's clothing, and the reported extent of teaching various skills and tasks to preschool age children by family members. In previous analyses, these three items showed consistent associations with birthweight.[30]

Weight of the newborn was determined within the first 24 hours of birth to the nearest 20 gm.

TABLE III

MAIN VARIABLES USED IN THE PRESENT ANALYSIS

No.	Variable
1	Maternal ingestion of food during pregnancy: experimental treatment, food supplementation (calories); daily home diet at ends of second and third trimesters
2	Maternal anthropometry during pregnancy: height and head circumference (at any time); weight (at end of first trimester)
3	Obstetrical history: parity, gestational age, birth interval, maternal age, and lactation during present pregnancy
4	Morbidity during pregnancy: composite indicator based on duration of diarrhea, anorexia, and remaining in bed due to illness; cord blood IgM levels
5	Socioeconomic status of family: composite indicator based on house, clothing, and education
6	Information on the newborn: birthweight and sex

TABLE IV

COMPLETENESS OF DATA COLLECTION ON BIRTHWEIGHT PER YEAR OF THE PROGRAM*

Data	1969	1970	1971 to 1973	Total 1969 to 1973
Births†	168	157	326	651
Birthweight data collected	40	100	265	405
Percentage of births	24	64	81‡	62

*Routine data collection of birthweight started on June 1970.

†Nine pairs of twins and two cases with exaggerated variability (1,500 and 5,500 gm) excluded.

‡Of the 61 cases without birthweight data (1971 to 1973), 38 were children from mothers who left the villages during the first months of their pregnancy and came back several weeks after the baby was born. For mothers whose pregnancy was followed, the coverage of birthweight data was 92%.

Sample Size

A total of 671 births occurred during the four years of data collection (from January 1969 through February 1973) in the four villages. Twins (nine pairs) and two cases with extreme birthweights for their gestational age (1,500 and 5,500 gm) were discarded for the present analysis. The total caloric supplementation during pregnancy for these two cases was 700 and 1,000 calories, respectively. Of the remaining 651 children data on the independent and dependent variables, maternal supplementation during pregnancy, and birthweight, respectively, were available for 405 babies (62%). Also, 210 mothers had two or more successive pregnancies during the four-year study and birthweight and maternal supplementation data were available for 94 pairs of consecutive pregnancies.

Rates of birthweight data collection per year of the study are presented in Table IV. The lowest completion rates occurred in 1969 because routine data collection was not instituted until June 1970. After that, birthweight was not collected for 60 infants, 38 of these because their

TABLE V

RELATIONSHIP BETWEEN SUPPLEMENTED CALORIES DURING PREGNANCY AND HOME CALORIC INTAKE

Measure	For the Four Villages Value
Correlation (r)	−.015
Slope (b)	−3.1 home cal/100 supplemented cal
P	>.10 (NS)
No. of cases	357

For Two Levels of Caloric Supplementation

Measure	Group: Low-Supplement (<20,000 cal)	Group: High-Supplement (≥20,000 cal)	Difference Between the Means (HSG - LSG)	P
Home caloric intake (cal/day)	1,415 ± 443	1,374 ± 364	−41	NS
Supplemented calories during pregnancy	7,200 ± 6,221	42,001 ± 19,221	34,801	<.001
Total caloric intake (cal/day)*	1,458 ± 446	1,607 ± 380	149†	<.001
Birthweight (gm)	2,997 ± 471	3,114 ± 476	117	<.05
No. of cases	192	165		

*Estimated by adding the ratio supplemented calories divided by 180 days to the daily home caloric intake.
†Equivalent to 26,820 calories during the last two trimesters of pregnancy.

mothers left the village during their first months of pregnancy and did not return until several weeks after delivery. For mothers for whom it was possible to follow the entire pregnancy, the coverage between June 1970 and February 1973 was 92%. Finally, the numbers in the Tables and Figures fluctuate because measurement of some of the other variables was instituted at different times and because an occasional measurement was missed.

RESULTS

The contribution of supplemented calories to total nutrient intake during pregnancy was examined and subsequent analyses focused on the relationship between food supplementation during pregnancy and birthweight.

Effect of the Supplemented Calories on the Total Caloric Intake During Pregnancy

The goal of the food supplementation intervention was to increase the total caloric intake during pregnancy. Reference to Table V shows that the correlation between supplemented calories and home caloric intake was negative, although not significant. Table V also shows that the home caloric intake for two levels of caloric supplementation was not significantly different. Therefore, these analyses indicate that there was no association between caloric supplementation and home caloric intake and that the supplementation program produced a net increase in the total caloric intake. Finally, after combining for each mother the calories from the home diet and the food supplement, the high-supplement group had a total caloric intake significantly higher than the low-supplement group. The difference between both groups (149 calories/day) indicates that the average net increase in the total caloric intake was 26,820 calories during pregnancy.

Relationship Between Food Supplementation During Pregnancy and Birthweight

To explore the effect of food supplementation during pregnancy on birthweight, we first measured the magnitude of the association between caloric supplementation and birthweight within the *fresco* and *atole* villages. Next, we investigated whether or not the observed association between supplemented calories and birthweight was due to other maternal characteristics, to changes in rates of missing data, or to some undetected maternal factor producing a trend to heavier babies in high-supplement mothers. This last analysis was made exploring the association between changes in caloric supplementation during pregnancy and changes in birthweight within siblings of the same mother.

Magnitude of the Association Between Food Supplementation During Pregnancy and Birthweight—Table VI describes the relationship between caloric supplementation during pregnancy and birthweight. The increase in birthweight for the same amount of calories, or slope value, is not significantly different between *fresco* and *atole* villages. This Table also demonstrates that in the total population there was a significant correlation between caloric supplementation during pregnancy and birthweight ($P < .01$).

It should be noted that there was a significant difference ($P < .05$) between the slope values for the *fresco* and *atole* villages when total volume of supplement ingested during pregnancy was used as independent variable instead of the total amount of supplemented calories. Thus, the slope value for the *fresco* villages was very low (9 gm of birthweight per 10 liters) as compared with the slope for *atole* villages (19 gm of birthweight per 10 liters). Earlier analyses had shown similar differences when supplemented volume was used as independent variable,[31] a result due to the different concentration of calories in the supplements.

Another approach to estimating the magnitude of this relationship consists of examining the differences in birthweight between two groups of pregnant women regarding their level of caloric supplementation. Table VII shows that there existed a significant difference ($P < .025$) between the mean birthweight for two levels of caloric supplementation during pregnancy (low-supplement group, ≤ 20,000 calories; high-supplement group, ≥ 20,000 calories). Again, this analysis shows no significant difference between the caloric and the protein-caloric supplementation.

The limit (20,000 calories) used to separate the low-supplement group from the high-supplement group was selected because in previous analyses[28] the median caloric supplementation during pregnancy in the four villages was very close to 20,000 calories. In these analyses, we found that this limit predicted risk of delivering babies with low birthweight and therefore we were interested in

TABLE VI

RELATIONSHIP BETWEEN SUPPLEMENTED CALORIES DURING PREGNANCY AND BIRTHWEIGHT

Village	Correlation Value (r)	Slope Value* (gm of birthweight per 10,000 cal)	No. of Cases	P
Atole	.113	23	219	<.10
Fresco	.123	30	186	<.10
Totals	.135	29	405	<.01

*Slope for *fresco* greater than slope for *atole:* NS (by test of covariance).

testing the consistency of our previous findings. In addition, the division above and below 20,000 supplemented calories was further rationalized by the observation that this amount of calories was close to the increment of caloric expenditure produced during pregnancy in well-nourished mothers[32] and that it would be sufficient to produce an increment of 60 to 240 gm in the average birthweight of this population.[33] It should be noted that in Table V the difference between the mean supplemented calories for the low-supplement group and the high-supplement group was 34,801 calories.

Finally, one of the most important estimations of the magnitude of this relationship, from a public health point of view, is the change in the proportion of low-birthweight babies produced by the nutritional intervention. Figure 1 shows the percentage of low-birthweight babies for the two groups. It can be seen that this proportion is consistently lower in the high-supplement in both the *fresco* and the *atole* populations. Thus, the association between caloric supplementation during pregnancy and birthweight is such that the rate of low-birthweight babies among low-supple-

TABLE VII

RELATIONSHIP BETWEEN SUPPLEMENTED CALORIES DURING PREGNANCY AND BIRTHWEIGHT FOR TWO LEVELS OF CALORIC SUPPLEMENTATION

Group	Mean Birthweight: *Atole* gm	*Atole* No.	*Fresco* gm	*Fresco* No.	Total gm	Total No.
High-supplement (≥20,000 cal)	3,173	102	3,035	68	3,105	170
Low-supplement (<20,000 cal)	3,042	117	2,948	118	2,994	235
Total	3,107	219	2,992	186	3,049 (±469)	405

Analysis of Variance for Differences in Birthweight

Cells	*P*
High greater than low	<.025
Atole greater than *fresco*	<.025
Interaction	NS

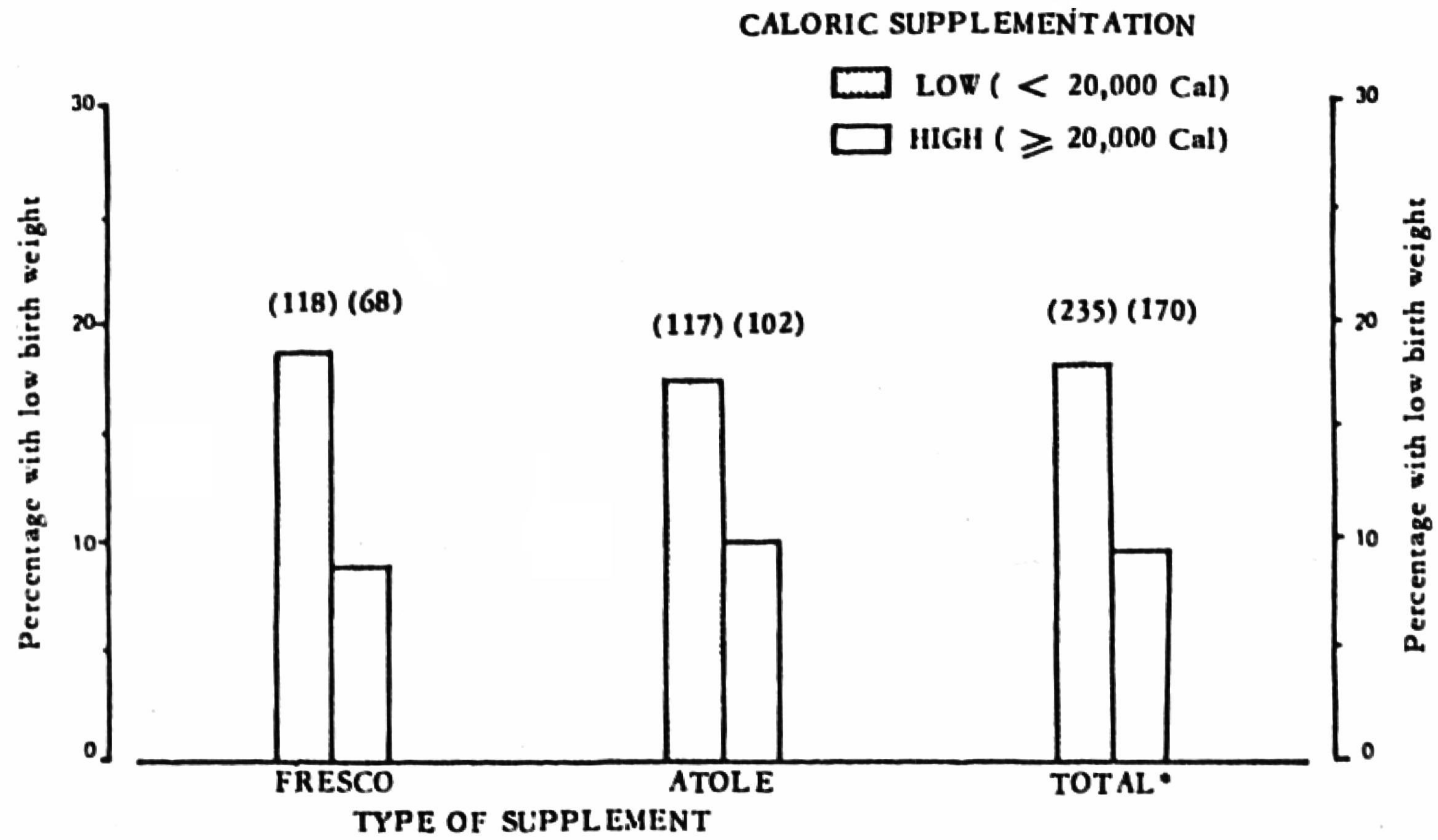

FIG. 1. Relationship between supplemented calories during pregnancy and proportion of low-birthweight (≤ 2,500 gm) babies. *Numbers in parentheses* indicate numbers of cases. *Asterisk,* $P < .05$.

ment mothers was roughly twice that observed among high-supplement mothers.

In summary, the analyses presented in Tables VI and VII and in Figure 1 indicate that there was a consistent association between supplemented calories and birthweight and that, provided that the same amount of calories was given, there were no significant differences between the protein-calorie and the calorie supplements.

Effect of Potential Confounding Factors—Once we detected a statistically significant association between caloric supplementation during pregnancy and birthweight, the question of primary interest was whether or not this association could be due to confounding factors. Thus, we explored the possibility that other maternal factors could be responsible for the observed association between supplemented calories and birthweight. By confounding factors we mean variables that are associated in the same direction with both the dependent (birthweight) and the independent (supplemented calories during pregnancy) variables. For example, it is possible that the high-supplement mothers were taller than the low-supplement mothers. Given the fact that taller women deliver heavier babies,[15,34] heights of the mothers could be responsible for the observed association between supplemented calories and birthweight. If this were the case maternal height would be a confounding factor.

The variables presented in Table III were investigated, first with respect to their association with birthweight and then with respect to their relationship with caloric supplementation during pregnancy. The correlation values between maternal characteristics and birthweight for those variables which were significantly associated with birthweight are presented in Table VIII. It can be seen that, in addition to caloric supplementation during pregnancy, gestational age, height, head circumference, socioeconomic status, chronological age, parity, weight at the end of the first trimester of pregnancy, and maternal morbidity were correlated with birthweight. However, none of these maternal characteristics were significantly correlated with caloric supplementation and, therefore, they cannot be responsible for the observed association between supplemented calories and birthweight.

Nevertheless, we explored through multiple regression analyses to what extent the original relationship between supplemented calories and birthweight reported in Table VI changed after controlling for the influence of the maternal variables presented in Table VIII. When these maternal factors were entered as independent variables in a multiple regression predicting birthweight, the dose-response relationship between caloric supplementation and birthweight remained statistically significant. Table IX shows that the relationship between supplemented calories during pregnancy and birthweight was basically unchanged after statistically controlling for the influence of these maternal variables.

Therefore, this analysis indicates that the maternal characteristics here measured, either alone or combined, could not explain the originally observed association.

In a previous review of the published literature on experimental and nonexperimental studies in humans, we arrived to the conclusion that, if there is an effect of food supplementation during pregnancy on birthweight, the expected magnitude for this effect should range between 25 and 84 gm of birthweight per 10,000 supplemented calories, depending on the previous nutritional status of the mother, home diet intake, grade of replacement of the home diet by the supplementary food, health status, and level of physical activity during pregnancy.[33] The slope values observed in Table IX (29 or 30 gm of birthweight per 10,000 supplemented calories) fall within the range of these expected dose-response relationships.

The distribution of these maternal factors for the low-supplement and high-supplement groups was also examined. Table X presents the mean and standard deviations of each of the maternal characteristics for two levels of caloric supplementation. It can be seen in this Table that there were no significant differences between the two groups for maternal height, head circumference, parity, and gestational age, but that there were significant differences between the groups for socioeconomic status and for the duration of morbidity during pregnancy. However, these variables cannot be responsible for the increment in birthweight observed in the high-supplement group since this group scored lower in the socioeconomic indicator and suffered more duration of disease during pregnancy than did the low-supplement group. Since birthweight decreases as duration of morbidity increases or as the socioeconomic score decreases (Table VIII), the birthweight increment found in the high-supplement group can not be explained by the differences observed in the socioeconomic score and in morbidity.

Effect of Missing Data—Table IV shows that the coverage for birthweight and maternal supplementation was 62% for the entire sample. This relatively low coverage was mainly due to the fact that systematic data collection on birthweight started 1½ years after the food supplementation program began (see section on sample size). To determine whether the observed association presented in Table VI and Figure 1 was due to bias produced by missing data, we examined this relationship in the population studied from July 1970 through February 1973, in which the data

TABLE VIII

MATERNAL DETERMINANTS OF BIRTHWEIGHT IN FOUR RURAL VILLAGES OF GUATEMALA

Determinant	*Correlation Coefficient*	*No.*
At conception		
Height	.134*	399
Head circumference	.284*	363
Age	.116*	401
Parity	.154*	404
Socioeconomic status indicator	.219*	363
At end of first trimester		
Weight	.277*	221
During pregnancy		
Gestational age	.217*	395
Morbidity indicator	−.122†	240
Caloric supplementation‡	.135*	405

*$P < .01$.
†$P < .05$.
‡Value for the multiple correlation predicting birthweight: $r = .410$ ($P < .01$).

TABLE IX

RELATIONSHIP BETWEEN CALORIC SUPPLEMENTATION DURING PREGNANCY AND BIRTHWEIGHT (No. = 405)

*Controlling for Suspected Confounding Factors**	*Slope†*	*SE*
Before (simple regression)	29	10.6
After (multiple regression)	30	10.6

*Height, head circumference, age, parity, socioeconomic status, weight at end of first trimester, gestational age, morbidity indicator, and home diet.
†Slope is obtained by dividing grams of birthweight by 10,000 calories. $P < .01$.

coverage was 92%. It can be seen in Table XI that in this population the relationship between supplemented calories during pregnancy and birthweight was similar in direction and magnitude to that observed in the whole study population. In addition, the slope value after controlling for the maternal factors presented in Table VIII was identical to that observed for the whole population after a similar procedure was applied. Therefore, it is unlikely that these findings are due to a bias produced by missing data.

Sibling Analysis—There remains the possibility that the mothers delivering heavier babies were those who also tended to collaborate more with the program. If this were the case, the association observed between caloric supplementation during pregnancy and birthweight would be artifactual. To explore the possibility that some constant

TABLE X

MATERNAL CHARACTERISTICS FOR TWO LEVELS OF CALORIC SUPPLEMENTATION DURING PREGNANCY

Maternal Characteristics	*Low-Supplement Group (<20,000 cal)*	*High-Supplement Group (≥20,000 cal)*	*P*
Height (cm)	148.9 ± 5.0	149.5 ± 5.5	NS
Birthweight (gm)	2,991 ± 457	3,118 ± 475	<.01
No.	229	170	
Head circumference (cm)	51.0 ± 1.4	51.0 ± 1.4	NS
Birthweight (gm)	3,000 ± 463	3,120 ± 478	<.05
No.	200	163	
Age (yr)	27.3 ± 7.3	28.1 ± 7.2	NS
Birthweight (gm)	2,994 ± 459	3,118 ± 425	<.05
No.	231	170	
Parity (No. of previous deliveries)	3.7 ± 3.4	4.1 ± 3.2	NS
Birthweight (gm)	2,993 ± 458	3,118 ± 475	<.01
No.	234	170	
Socioeconomic status indicator	0.96 ± 0.83	0.75 ± 0.84	<.05
Birthweight (gm)	2,998 ± 460	3,116 ± 484	<.05
No.	205	158	
Weight at end 1st trimester (kg)	48.1 ± 5.8	48.4 ± 6.9	NS
Birthweight (gm)	3,093 ± 508	3,117 ± 480	NS
No.	91	130	
Gestational age (wk)	39.6 ± 1.6	39.7 ± 1.5	NS
Birthweight (gm)	2,997 ± 459	3.118 ± 479	<.05
No.	229	166	
Morbidity indicator (days/month of pregnancy)	2.1 ± 3.3	3.1 ± 4.7	<.05
Birthweight (gm)	3,025 ± 487	3,106 ± 491	NS
No.	96	144	

maternal factor might be responsible for both the high consumption of food supplement during pregnancy and heavier newborns, we studied consecutive siblings of the same mother.

Figure 2 presents the mean differences in birthweight for 94 pairs of siblings divided into three groups. These groups were defined by the differences in caloric supplementation of the mother between two successive pregnancies. When caloric supplementation during the latter pregnancy was lower than during the preceding pregnancy, the birthweight of the latter baby was lower than that of the preceding baby. When the caloric supplementation during the latter pregnancy was more than 20,000 calories higher than during the preceding pregnancy, the latter newborn was heavier than the preceding one. The intermediate group is composed of siblings in which the increment in caloric supplementation during the latter pregnancy was between 100 and 20,000 calories. In this group, the mean difference in birthweight between both babies was close to zero and, therefore, intermediate between the extreme groups. In consequence, the analysis presented in Figure 2 indicates a positive association between changes in caloric supplementation and changes in birthweight in consecutive pregnancies of the same mother. The correlation between differences in caloric supplementation between both pregnancies and differences in birthweight between both babies was also significant (r = .298; No. = 94, $P < .01$). Finally, after adjusting the changes in caloric supplementation and in birthweight for the intercorrelations existing between successive pregnancies,* the relationship between caloric supplementation and birthweight was roughly similar (slope value = 22 gm of birth weight per 10,000 calories) to that observed in the entire population.

In summary, the analyses presented in Tables VIII to XI and in Figure 2 indicate that the relationship of supplemented calories to birthweight was consistent in the entire population studied, in the population with the highest rates of coverage, and between siblings of the same mother.

*Successive birthweights are correlated (r = .549; $P < .001$) as is the amount of caloric supplementation between two successive pregnancies (r = .414; $P < .001$).

TABLE XI

RELATIONSHIP BETWEEN SUPPLEMENTED CALORIES AND BIRTHWEIGHT IN REGARD TO DIFFERENT RATES OF COVERAGE ON BIRTHWEIGHT DATA

Population	Coverage Rate (%)	Correlation Value (r)	Slope*		No. of Cases
			Simple Regression	Multiple Regression	
Total (21,812 ± 21,770)†	63	.135	29§	30§	405
High coverage‡(24,407 ± 22,649)†	92	.116	24‖	30§	331

*Slope was obtained by dividing grams of birthweight by 10,000 calories after controlling for suspected confounding factors: height, head circumference, parity, socioeconomic status, weight at end of first trimester, gestational age, morbidity indicator, and home diet. Slope for total study population was not significantly greater than slope for high coverage population by test of covariance.

†Numbers in parentheses indicate mean caloric supplementation ± SD.

‡From July 1970 through February 1973.

§$P < .01$.

‖$P < .05$.

DISCUSSION

We have found an association between supplemented calories during pregnancy and birthweight and also the somewhat surprising result that both the protein-calorie and the caloric supplements had a similar effect on birthweight. In the following paragraphs we will discuss some of the questions of logic raised by these results: the possible explanations for the absence of effect of protein supplementation on birthweight; the cause-and-effect nature of the observed association, and the potential public health implications of these findings.

Why Was There No Effect of Protein Supplementation on Birthweight?

There are several explanations for the unexpected result that protein supplementation was not directly associated with birthweight. First, in this population the main limiting nutrient in the maternal home diet is calories and not protein. The average home caloric intake is very low and provides a relatively small margin for physical activity (around 250 calories). On the other hand, protein intake from home diet is slightly higher (7.5%) than the average required for maintenance and tissue synthesis.[33] Also, the protein to calorie ratio in the home diet (11.5%) is similar to the observed figures for well-nourished populations.

An analysis of the literature suggested that, if the hypothesis of caloric limitation is correct, an increment of 20,000 calories in the total caloric intake during pregnancy would produce an average daily retention of 0.72 gm of nitrogen per day, which is enough to produce a birthweight increment from 72 to 168 gm as well as the associated weight gain during pregnancy. Under similar conditions of caloric limitation, a very large increment of the protein intake would be required to produce a similar value in nitrogen retention and the same increment in birthweight. Above a certain limit of caloric supplementation, protein will gradually become the main limiting factor. In this case, further caloric supplementa-

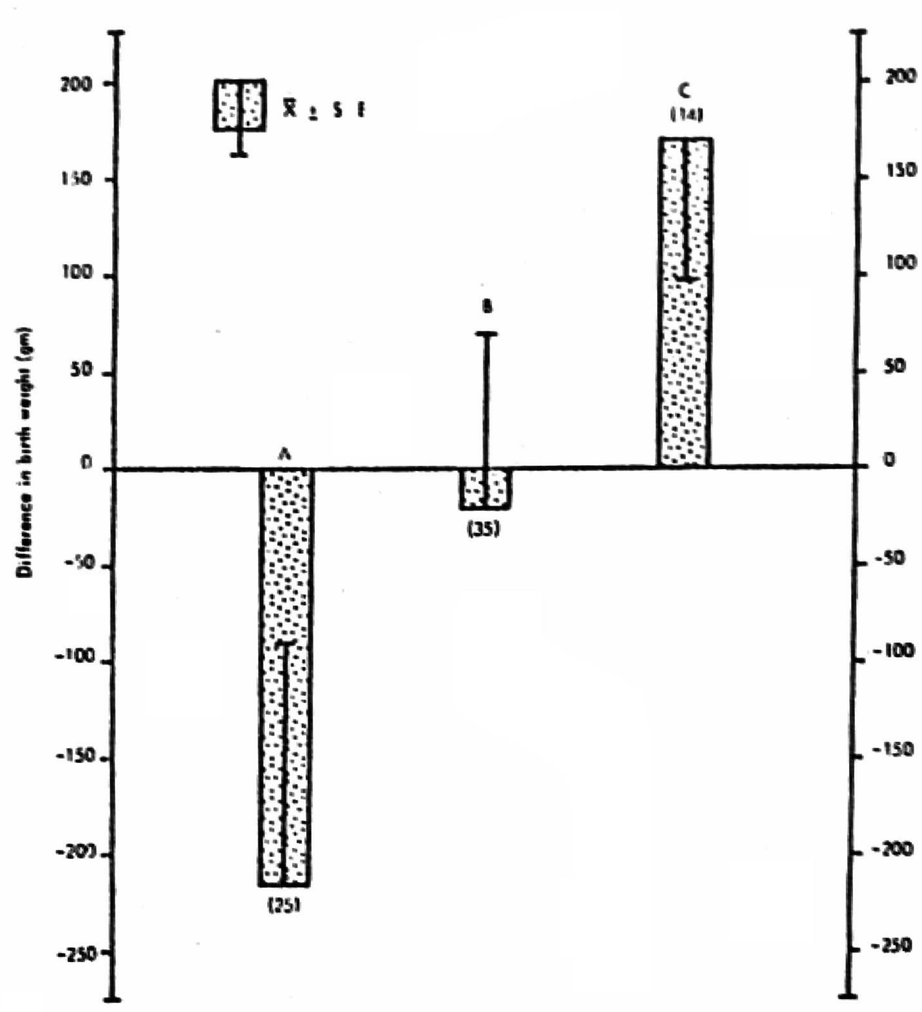

FIG. 2. Relationship between differences in caloric supplementation and differences in birthweight for two consecutive siblings (second birthweight minus first birthweight). No. = 94 pairs. Difference in caloric supplementation during pregnancy: $A = -40{,}000$ to 0 calories; $B = 100$ to 20,000 calories; $C = 20{,}000$ to 120,000 calories. *Numbers in parentheses* indicate numbers of pairs. Difference between A and C: $P < .01$.

tion alone would not produce an effect on birthweight unless it was accompanied by protein supplementation.[33]

Other factors are also important in explaining the observed effect of caloric supplementation and they are discussed elsewhere.[33] The most likely to us are that the human fetus may adapt better to protein deficiency than to caloric deficiency and that, within the range of mean birthweight under discussion (3,000 to 3,200 gm) birthweight would mainly be a function of the accumulation of fetal adipose tissue and therefore of the availability of calories.[33]

Is the Relationship Between Caloric Supplementation and Birthweight a Causal Association?

Experimental studies are best suited to make causal inferences. However, our experiment was originally designed to test the effect of protein supplementation, not caloric supplementation, on birthweight. Thus, two villages were assigned to the group supplemented with protein and calories and the other two were supplemented with the caloric preparation. The main weakness in this design is that, because the experiment was not designed to test the effect of levels of caloric supplementation during pregnancy on birthweight, the allocation of the pregnant women in a particular category of caloric supplementation was based on their cooperation with the food supplementation program and not on a planned action of the researcher. Therefore, we should interpret the observed results not in terms of an experiment, but as a finding from a nonexperimental, prospective, cohort study in which the exposure (caloric intake) and outcome (birthweight) were carefully assessed, and one in which important maternal factors could not explain the detected association between supplemented calories and birthweight.

From this point of view, the analyses presented here have shown that:

(1) The caloric supplementation produced a biologically significant increment in the total nutrient intake during pregnancy.

(2) Higher levels of caloric supplementation during pregnancy were associated with a significant increase in birthweight and a decrease of the risk of delivering low-birthweight babies.

(3) There was a dose-response relationship of a similar order of magnitude to that computed from a wide variety of studies.

(4) This association with birthweight held constant after important maternal variables were controlled.

(5) The relationship was not due to missing data.

(6) In addition, this association was not produced by undetected confounding factors related to the mother (such as an individual tendency to have bigger babies) since it was also observed within two consecutive siblings of the same mother.

Therefore, we concluded that the most suitable interpretation of these results is that caloric supplementation during pregnancy *caused* an increase in birthweight in this population.

What Are the Public Health Implications of These Findings?

The ultimate implications of the observed association depend on the importance of birthweight *per se* for the baby. We mentioned at the beginning of this paper that low-birthweight babies have higher rates of infant and neonatal mortality and are more likely to perform poorly on tests of mental development than are babies with higher birthweights. In the United States most of the differences in infant mortality rates between whites and non-whites are directly associated with differences in birthweight.[2] Further analyses based on the data of Chase[2] demonstrated that the impact of an improvement of maternal nutrition on infant deaths would depend on the extent to which such a program produces a decrease on the proportion of low-birthweight babies.[35] This suggests that the efficiency (or benefit to cost ratio) of nutritional programs aimed at decreasing infant mortality could be greatly enhanced if these programs were focused on mothers at high risk of delivering low-birthweight babies. For this purpose, several risk instruments feasible for use in populations with inadequate health services have been recently proposed.[36,37]

In conclusion, the observed effect of food supplementation during pregnancy on birthweight presents important public health implications in terms of the possibility of decreasing infant mortality rates in many poor communities around the world.

It should be emphasized that this technique of nutritional intervention, by distributing a food supplement, was implemented as a research manipulation. Food supplementation programs generally are expensive and time-consuming, create "dependent" populations, and frequently induce unfavorable effects on the local food industry. Therefore, they are inappropriate for large populations over long periods of time. Since the causal association between maternal nutrition and birthweight is deeply immersed in the surrounding socioeconomic context,[30] improvement of specific socioeconomic factors such as family income and purchasing power for basic foods might be more effective and efficient than the traditional interventions based on food supplementation programs. We know little about intervention techniques of that nature and for this reason much more attention should be devoted to the evaluation of those programs which aim to break the vicious circle of socioeconomic deprivation, maternal malnutrition and impaired intrauterine development.

FINAL COMMENTS

In summary, from the published literature as well as from our own data, we believe that an improvement in the nutritional status of pregnant women will lead to a significant decrease of the prevalence of low-birthweight in most poor communities. This in turn would help to reduce the high rates of infant mortality in these societies and would provide new generations a better chance to achieve their full genetic potential.

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