RELATIONSHIPS OF BIRTHWEIGHT, MATERNAL NUTRITION AND INFANT MORTALITY[1]

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ABSTRACT

Calorie supplementation during pregnancy is associated with heavier babies in a rural Guatemalan sample. This paper outlines other possible maternal and environmental factors related to birthsize and suggests that increased birthweight is the prime factor in reducing infant mortality among babies born to supplemented mothers. Caloric supplementation during pregnancy has less effect on birthweight than do maternal height and weight at conception, indicating that efforts to improve maternal nutrition should begin in childhood for optimum infant survival, and that during pregnancy, small thin mothers should be supplemented to prevent the birth of "small for date" babies.

INTRODUCTION

In 1969, we began a longitudinal study of the social and biological determinants of physical growth and mental development in rural Guatemala. Since that time, we have provided food supplements to pregnant women. The purpose of this paper is first to review our findings showing an association between maternal calorie supplementation during pregnancy and increased birthweight, as well as our reasons for believing that this association is one of cause and effect. Secondly, we will present and discuss a provisional model which we are using to guide further investigation of the various factors affecting infant birthweight and postnatal development. Finally, we will present two examples of research findings with postnatal implications which derive from the use of this model.

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Elsewhere we have presented evidence for an association of birthweight with maternal caloric supplementation during pregnancy (1). Birthweights were found to increase about 50 grams for each ten thousand calories of supplement ingested during pregnancy. This increase was observed up to about 30,000 calories and was found throughout the entire range of birthweight[1]. The increase in birthweight associated with maternal supplementation was equally strong and of similar magnitude regardless of when during pregnancy the supplement was ingested (2). Finally, protein added to the caloric supplement did not increase birthweight significantly, in spite of the fact that home diets are limiting in proteins for preschool children (1).

Inference of a cause-effect relationship for this association of maternal calorie supplementation during pregnancy with birthweight, requires that we must eliminate alternative explanations.

This is important because differential drop-out rates or variations in subject cooperation rates can result in supplemented and unsupplemented subject groups of different composition, even though initially they were similar by assignment. If for instance, one supplement is nutritious and another is not, differential physiological responses to the two supplements could affect factors such as which women cooperate, as well as how much each woman consumes.

Therefore, the logic of data analysis is as important as the experimental design if we are to forestall erroneous conclusions from the experimental findings. With this in mind, I will review our experimental design.

METHODS

In two villages, a protein and calorie supplement, "atole"[2] is given, whereas, in two other villages a calorie supplement, "fresco"[3], is provided. The calorie concentration by volume of the "fresco" is about 1/3 the calorie concentration of the "atole". These supplements are available twice daily in central

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1 Premature babies (∠37 weeks of gestation (4.1%) of the sample and twins (2.5%) of the sample were not included in these analysis.

2 "Atole": The name of a gruel commonly made with corn.

distribution centers where attendance is voluntary. The amount ingested is unrestricted and it is recorded to the nearest centiliter. Birthweight is measured to within 20 grams during the first day of life by personnel who are ignorant of the amount of supplement ingested by the mother.

RESULTS AND DISCUSSION

To invoke nutritional mechanisms to explain the association between the birthweight and supplementation we must exclude other explanations. At very least, factors known to have a strong effect on birthweight must be taken into account. These include maternal height, weight, age or parity, smoking, duration of gestation and sex of the infant (3).

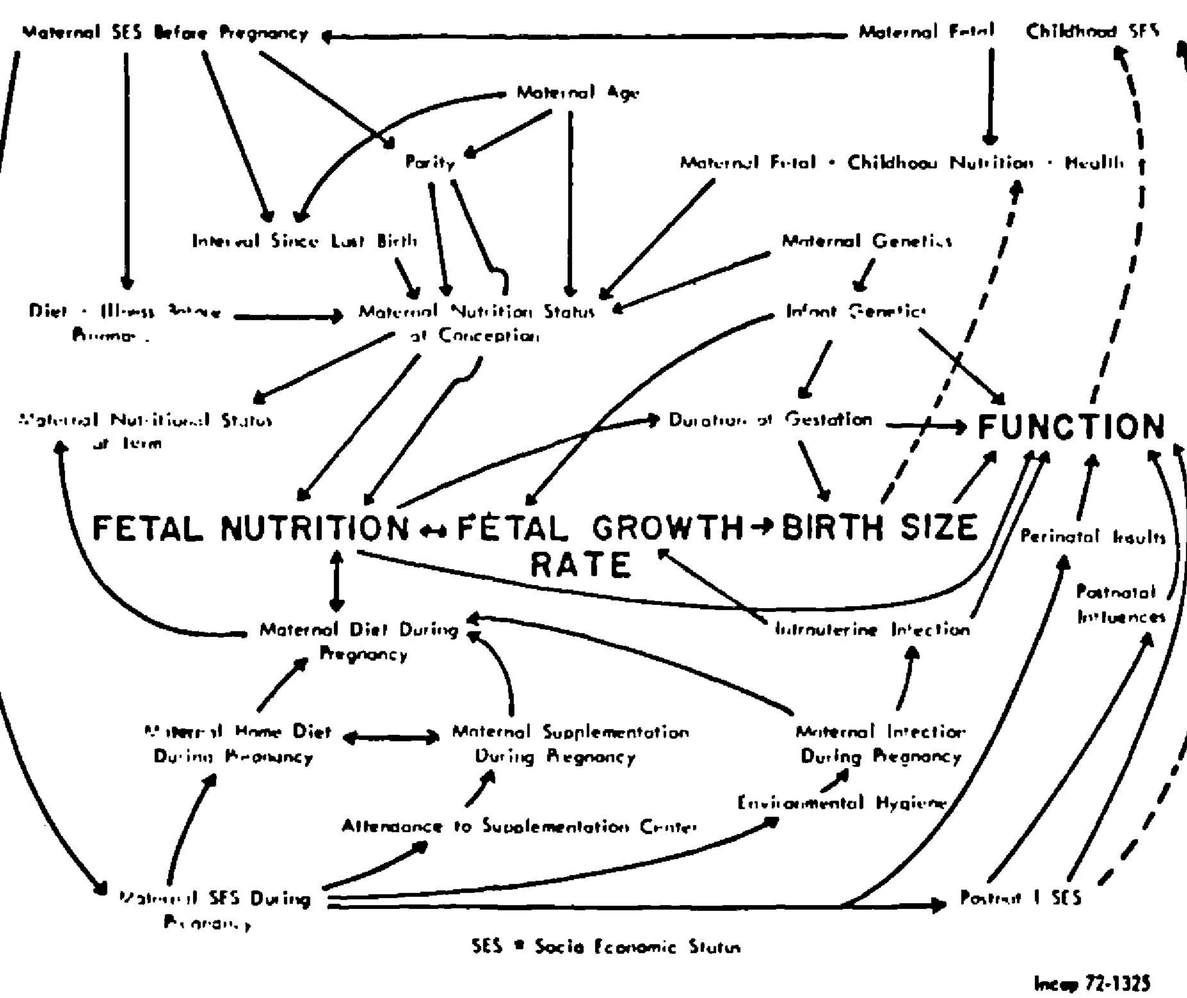

Fig. 1. Postulated influences on birth size and postnatal function (Overall View).

Figure 1 presents a working model which reflects our present suppositions about the relation between various prenatal factors, birthsize, and postnatal function in our study villages. The operational description of these factors is presented in Table I.

Table I

OPERATIONAL MEASUREMENTS OF CONCEPTS IN FIGURE 1

Concept	Operationalization	Observations
Fetal Nutrition	Gestational age specific Birth size (Biochemistry of placenta and cord blood),	
Birth Size	Birthweight, length (muscle and fat mass)*	Within 24 hours to ± 20 grams
Function	Infant mortality (postnatal growth, neurological and psychological performance)	Within 24 hours of death
Duration of Gestation	Weeks since last menstruation	Presence or absence of menses recorded every two weeks
Infant Genetics	Sex (Blood groups)	
Parental Genetics	(Blood groups, parental and sibling anthropometry, family history)	
Perinatal Insults	Birth history	Recorded by trained observer
Intrauterine Infection	Cord immunoglobulin M levels (Specific antibody levels and isolation of infective agents)	
Maternal Infection	Days of illness during pregnancy.	By recall every two weeks.
Home Diet	Ingestion of calories and other nutrients	In 2nd., 5th & 8th months by recall survey. Precision standard deviation ± 250 Kcal.

TABLE I (continued)

Concept	Operationalization	Observations
Supplementation	Ingestion of calories and other nutrients	Per visit, to ± 9.1 Cal. for Atole and to ± 3.3 Cal. for Fresco.
Attendance to Supplementation Center	Number of days attended during pregnancy	Recorded every day.
Maternal Nutritional Status	Maternal weight for height (muscle and fat mass per height)	In 2nd. month of pregnancy to ± 100 grams.
Maternal Age	Years of age	Recall and civil registry.
Parity	Number of children born	Recall, civil registry, census
Interval between births	Measured in months	
Socioeconomic Status	Quantity of home teaching, quality of the house	See:footnote
Upbringing	(Mother/child interaction)	

* Parentheses indicate data not yet available

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The most important determinants of birthsize, according to Figure 1, are the rate of fetal growth and duration of gestation.

Fetal growth rate, in turn, is affected by certain kinds of intrauterine infections (4), by sex, and possibly other infant genetic factors. It is clear from this schema that we do not expect any paternal influences on birthweight, except from chromsomal abnormalities. The fetal growth rate probably has a reciprocal relationship with the nutrition of the fetus. A faster growing fetus makes greater nutritional demands than a slower growing fetus, while inadequate nutrition will slow the rate of fetal growth. Smoking is so rare, among women of child bearing age in the study villages, that smoking is not included in Figure 1.

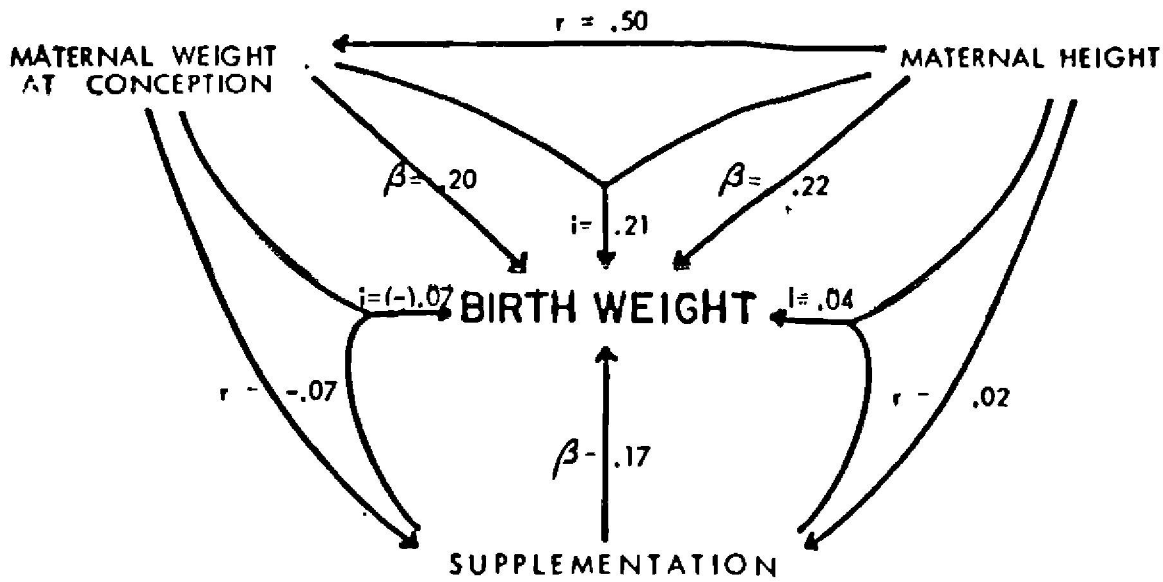
Some intrauterine infections can cause intrauterine growth retardation, whereas, others can cause functional damage without any other symptoms (5). Intrauterine infection is usually preceeded by infection of the mother which in turn may affect maternal appetite during pregnancy and hence diminish maternal food intake. Maternal infections are more common where poor environmental hygiene is prevalent. Poor environmental hygiene is but one reflection of the miserable rural socio-economic conditions (SES) which also affect home diet and attendance to the supplementation centers. Supplement ingestion appears to have a reciprocal relationship with amount of calories ingested in the home and is affected by attendance to the supplementation centers.

The nutrition of the fetus is not only influenced by maternal diet during pregnancy but also by the mother's previous nutritional status reflected by her weight at conception.

Parity can affect the fetal nutrition directly by changes in the uterus, as well as indirectly through changes in maternal nutritional stores. These maternal stores are further affected by maternal age and the rapidity with which one birth follows another.

Nutrition and health before pregnancy affect the mother's caloric nutritional status at conception and would be expected to influence maternal nutritional demands during pregnancy. Prepregnancy diet and illness, in turn are influenced by the prepregnancy socio-economic environment of the mother. These socioeconomic factors also influence the childbearing practices of the mother.

These kinds of influences will ultimately affect the birthweight of babies born in the future to this baby and are represented by dotted arrows in Figure 1.



LEGEND: r = Correlation Coefficient (Snedecor, 1967, p. 172).
β – Standard Partial Regression Coefficients (Snedecor, 1967, p. 398)
i^2 = Interaction Term = $2\beta_1 r_{12} \beta_2$; (–) = i^2 negative
r^2, β^2 and i^2 are directly comparable as all are expressions of the explanatory power of the variables on the variance of birth weight
N = 152

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Fig. 2. Relative importance of maternal height, weight, and supplementation on birth weight.

Figure 2 illustrates the relative importance on birthweight of each of the three variables: maternal weight at conception, maternal height and maternal caloric intake from supplementation during pregnancy. The independent contributions (β) to birthweight variance is similar and statistically significant ($P < 0.05$) for each of the three variables, as is the common contribution (i) of maternal height and weight at the inception of pregnancy. On the other hand caloric supplementation during pregnancy affects birthweight almost independently of both maternal height and weight. It is of interest, however, that the interaction of supplementation with the two maternal variables, height and weight, are in the direction expected for physiological reasons. The taller the mother the greater her caloric intake will be, while the greater the weight (for the same height) of the mother at conception the less will be her caloric needs during pregnancy to produce a healthy baby.

In the villages from which this sample is drawn, we have shown that childhood growth, especially in height, is affected by differences in nutrition (2). We may therefore, assume that the present height of these mothers was determined in large measure by their childhood nutrition. Figure 2 presents strong evidence that this childhood nutrition is as important a determinant of birthweight as is caloric supplementation during pregnancy. Similarly, if maternal weight differences, given a similar height, are due to differences in nutrition before pregnancy, this nutritional status of the mother at conception is as powerful a determinant of birth weight, as is caloric supplementation during pregnancy.

Past obstetrical history and maternal age which also affect birthweight, do not affect these interrelationships among birthweight and maternal height, weight at conception and maternal supplementation. Our next task is to include more variables in this type of analysis to further illuminate the mechanisms influencing birthweight.

Another example of the use of the hypothetical model illustrated in Figure 1 is a consideration of postnatal function of the child. Ultimately, we hope to elucidate the role each prenatal influence plays on the infant and preschool child's physical growth and mental development. For the present discussion we have chosen the most trenchant measures of postnatal function; does the baby survive infancy or not.

Figure 1 presents several prenatal factors which may affect infant mortality. Here we ask whether these prenatal factors influence infant mortality independently of each other, as well as, what are the relative importance of these various factors in infant survival?

Fetal nutrition can possibly affect chances of survival through increased birthweight or through some improvement in some other indices of fitness independent of birthweight. We chose maternal calorie supplementation during pregnancy as the measure of maternal nutrition, because maternal supplementation is the only nutritional factor affecting birthweight, which we know is not positively confounded with socio-economic status (1). This is important because, if we show a reduction in infant mortality associated with maternal supplementation, one must be able to exclude the possibility that postnatal factors linked to socio-economic status are involved.

Table II shows that infant mortality in the study villages is four times greater for babies whose birthweight is 2.5 Kg. or less at term ("small for date babies") than for heavier babies

($P < 0.05$). Although the numbers to date are small, this difference is so large that it is undoubtedly of biological importance.

TABLE II
RELATIONSHIP OF INFANT MORTALITY TO BIRTHWEIGHT

Birthweight	Children Born*	Deaths+	Infant Mortality Rates Per 1,000	
≤ 2.5 Kg.	33	4	121	
2.6-3.0 Kg.	90	6	67	30
> 3.0 Kg.	107	0	0	

* Between January 1, 1969 through October 27, 1971 = Infants at Risk.

\+ Deaths of infants at risk from January 1, 1969 through October 27, 1972.

TABLE III
COMPARISON OF CALORIC INGESTION FROM MATERNAL SUPPLEMENTATION WITH BIRTHWEIGHT DISTRIBUTION

Birth Weights	AMOUNT OF CALORIES INGESTED FROM SUPPLEMENTATION DURING PREGNANCY		
	Less Than 5,000	5,000-19,999	20,000 or more
	N = 82	N = 89	N = 117
	Percent Birthweight Distribution		
> 3.0 Kg.	41.5%	41.6%	54.7%
2.6-3.0 Kg.	37.8%	40.4%	40.2%
≤ 2.5 Kg.	20.7%	18.0%	5.1%

Table III shows how by increasing maternal calorie supplementation during pregnancy the number of babies weighing 2.5 Kg or less is reduced from 20% among babies born to mothers ingesting less than 5,000 calories during pregnancy to 5% among babies born to mothers who consumed more than 20,000 calories during pregnancy.

Figure 1 indicates, however, that nutrition is only one factor affecting birthweight. We could imagine that infant mortality is not determined by birthweight, but by the cause of the low birth weight. If this were true, genetic defects and intrauterine infection could be the causes of the high infant mortality and these lethal factors are identified as L in Table IV.

TABLE IV

CALCULATION OF CHANGES IN INFANT DEATH RATES OF "SMALL FOR DATE" BABIES AS FETAL NUTRITION IMPROVES IF FETAL MALNUTRITION IS NOT A CAUSE OF DEATH

	WITHOUT	WITH
	MATERNAL SUPPLEMENTATION DURING PREGNANCY	
Number of babies weighing less than 2.5 Kg. who will die within the year.	L	L
Number of babies weighing less than 2.5 Kg. who will survive at least a year.	B + N	B
Total babies born weighing less than 2.5 Kg.	L + B + N = 20%	L + B=5%

Expected increase in infant death rate=

$$\frac{L}{L+B} \div \frac{L}{L+B+N} = \frac{L+B+N}{L+B} = \frac{20}{5} = 4 \text{ fold}$$

Legend:

L = Lethal factor producing babies weighing less than 2.5 Kg. at birth who will die within the year.

B = Non-lethal, non-nutritional factors producing babies weighing less than 2.5 Kg. at birth who will survive at least a year.

N = Non-lethal, nutritional factors producing babies weighing less than 2.5 Kg. at birth, who will survive at least a year.

In this context, birthweight would only be an index of congenital adversity.

In contrast to intrauterine stunting due to lethal factors, "small for date" babies caused by poor maternal nutrition may well have no increased infant mortality over heavier babies. "Small for dates" due to maternal malnutrition are labelled N in Table IV. Fetal malnutrition ceases at birth, while the repercussions of genetic defects and intrauterine infection would continue into infancy. If through better maternal nutrition no nutritionally stunted babies are born, then the remaining "small for date" babies would be caused by the other lethal (L) and benign (B) factors. The lethal factors would, in turn, directly cause infant death. If this hypothesis is true, Table IV outlines how infant mortality among the "small for date" infants should then rise as the proportion of "small for date" babies decreases from 20% to 5%.

TABLE V
RELATION OF INFANT MORTALITY TO MATERNAL SUPPLEMENTATION DURING PREGNANCY AND BIRTHWEIGHT

Birthweight	MATERNAL CALORIC SUPPLEMENTATION	
	$<$ 20,000 Calories	$\geqslant$ 20,000 Calories
$\leqslant$ 2.5 Kg.	4/30 = 133*	0/3
$>$ 2.5 Kg.	4/115 = 35	2/82=24

* Infant deaths°/Infants at Risk+ = Infant mortality/1,000 births.

° Infant Deaths = Deaths of infants at risk from January 1, 1969 to October 27, 1972.
+ Infants at Risk = Born from January 1, 1969 to October 27, 1971.

Table V shows that this does not happen for we would have expected at least two of the three "small for date" babies born to well supplemented mothers to die.

Finally, improved maternal nutrition could conceivably neutralize the birth weight reduction caused by a lethal factor, which under usual village conditions would have resulted in a "small for date" baby. We would expect then to see a rise in infant mortality among the babies larger than 2.5 Kg. born to supplemented mothers. Thus, among the 85 infants of well supplemented mothers, an estimated 18 infants (85 x 30/145) would have been "small for date" had their mothers not been supplemented. We would have expected 2 to 3 deaths among these 18 infants. Of the children who would have not been "small for date" under usual village conditions, we would have expected at least 1 death. Thus, we would have expected from 3 to 4 deaths among the infants of well supplemented mothers who weighed over 2.5 Kg. Table V shows that this did not happen. This is consonant with the notion that the main determinant of infant mortality is low birthweight and not some independent mechanism of the cause of the low birthweight.

TABLE VI
RELATIONSHIP OF INFANT MORTALITY
TO MATERNAL SUPPLEMENTATION DURING PREGNANCY

Amounts of Supplement Calories Ingested During Pregnancy	Children* Born	Deaths[+]	Infant Mortality Rates
$<$ 5,000	71	4	56
5,000 - 19,999	74	4	54
$>$ 20,000	85	2	24

* Between January 1, 1969 through October 27, 1971 = Infants at Risk.

\+ Deaths of infants at risk from January 1, 1969 through October 27, 1972.

Table VI indicates how by increasing maternal supplementation during pregnancy the infant mortality decreases from 55 per 1,000 births among babies born to mothers who consume less than 20,000 calories during pregnancy, to 24* per 1,000 births among babies born to mothers who consume more than 20,000 calories during pregnancy. It is important to realize that this effect of supplementation on infant mortality is above and beyond that issuing from the medical care which is provided to both groups of mothers. This indicates that we can lower village infant mortality by ensuring adequate levels of maternal

* This is not comparable to the 22/1,000 U.S.A. infant mortality rate because the U.S.A. figure includes prematures (6).

nutrition during pregnancy among the mild to moderately malnourished women in our study villages.

CONCLUSIONS AND SUMMARY

We have presented an integrated quantitative approach to the analysis of data collected in a maternal supplementation program. Two examples of this approach are given. The first example compares the effects of maternal height and weight at conception, and maternal calorie supplementation during pregnancy on birthweight. We conclude that maternal childhood nutritional status and maternal nutritional status immediately preceding pregnancy are as important determinants of birthweight as is maternal nutrition during pregnancy.

The second example presents evidence that maternal malnutrition during pregnancy might explain much of the difference in infant mortality between this Guatemalan sample and the U.S.A. The reduction in infant mortality which is produced by maternal caloric supplementation during pregnancy appears to be mediated through the increased birthweight of the newborn.

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