Twin pregnancy: the impact of the Higgins Nutrition Intervention Program on maternal and neonatal outcomes[1-3]

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ABSTRACT Perinatal outcomes were compared between 354 twins treated with the Higgins Nutrition Intervention Program and 686 untreated twins. After differing distributions of key confounding variables were adjusted for, the twins in the intervention group weighed an average of 80 g more ($P < 0.06$) than the nonintervention twins; their low-birth-weight rate was 25% lower ($P < 0.05$) and their very-low-birth-weight rate was almost 50% lower ($P < 0.05$). Although the rate of preterm delivery was 30% lower in the intervention group ($P < 0.05$), the rates of intrauterine growth retardation were similar in the two groups. Fetal mortality was slightly higher (14 vs 12 per 1000, NS), but early neonatal mortality was fivefold lower (3 vs 19 per 1000, $P < 0.06$) in the intervention group. Maternal morbidity was significantly lower ($P < 0.05$) in the intervention group. There was a trend towards lower infant morbidity in the intervention group. These results suggest that nutritional intervention can significantly improve twin-pregnancy outcome. *Am J Clin Nutr* 1991;53:1397–1403.

KEY WORDS Twin pregnancy, nutrition intervention, birth weight, morbidity, mortality

Introduction

Twin pregnancies are high-risk pregnancies (1–3). Perinatal mortality rates for twins are several times greater than for singletons, and morbidity rates are high among surviving twins (3–7). The intrauterine growth and development of twins and singletons are virtually identical until about 32 wk gestation. After that point there is an apparent deceleration of growth in twin pregnancies, resulting in increasing rates of intrauterine growth retardation (IUGR) among twins as pregnancies approach term (7–9). Twin pregnancies are also generally characterized by a shortened length of gestation, 37 wk on average as compared with 40 wk for singleton gestations (10). Associated with this 3-wk shorter average length of gestation in twins is a five- to tenfold greater incidence of preterm delivery (3).

Low-birth-weight rates, which are related to increased rates of both IUGR and preterm delivery, are five to ten times higher in twins than in singletons (3, 10–12). This high rate of low birth weight is believed to contribute substantially to the high mortality and morbidity rates of twins (3, 4, 11); birth-weight–specific morbidity and mortality rates are similar for twins and for singletons (3, 13). Hays and Smeltzer (3) proposed that the key to reducing the magnitude of the morbidity and mortality problem in twin pregnancies lies not in changing management procedures during labor and delivery (eg, increasing the Caesarean-section rate) but rather in taking measures during pregnancy to reduce the proportion of twins who are low birth weight.

In this regard it was suggested in several publications dealing with the obstetric management of women with multiple gestations that these women need to consume more food during pregnancy than do women with singleton gestations (3, 10, 12, 14, 15). However, despite the intuitive logic of encouraging greater food consumption when more than one fetus is present, there appear to have been no formal evaluations of the ability of such a preventive measure to improve multiple-pregnancy outcomes. In a single reference reporting food consumption in multiple gestations, Campbell et al (16) found that mean daily calorie and protein intakes at ~30 wk gestation were similar in a group of women with twin gestations and in a group with singleton gestations. These authors did not however report data on either birth weight or on the rates of adverse pregnancy outcome (eg, low-birth-weight rates, rates of IUGR or of perinatal morbidity or perinatal mortality) in the two groups.

To help clarify this somewhat contradictory situation, the present report describes the results of a study designed to evaluate the impact of the Higgins Nutrition Intervention Program on twin-pregnancy outcome. This report provides information about the extent to which birth weight can be increased and the risk for low birth weight, prematurity, IUGR, perinatal morbidity, and perinatal mortality can be decreased for twins whose mothers are treated with an individualized nutrition-intervention program.

Methods

The Higgins Nutrition Intervention Program

Developed at the Montreal Diet Dispensary as an adjunct to normal prenatal care, the Higgins Nutrition Intervention

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Method© of assessment and rehabilitation consists of an assessment of each pregnant woman's risk profile for adverse birth outcomes and an individualized nutrition-rehabilitation program based on that profile. The Higgins Nutrition Intervention Program, which consists of the systematic application by trained dietitians of all components of the Higgins method, was described in detail elsewhere (17). Four basic steps are involved in its implementation: *1*) assessment of the risks for the presenting pregnancy (**Table 1**) (18–20), *2*) determination of individual dietary requirements based on the combination of the normal requirements of pregnancy and rehabilitation allowances for diagnosed risk, *3*) teaching of food-consumption patterns that meet individual dietary requirements while respecting preexisting food habits, and *4*) follow-up and supervision by the same dietitian at 2 to 4-wk intervals. In addition, women judged unable to afford the prescribed diet by an income eligibility scale (21) are provided with a supplement of milk and eggs for the remainder of their pregnancy. All women are encouraged to stop smoking. Referrals are made to appropriate agencies for further assistance and follow-up of nonnutrition problems.

A unique feature of the Higgins program is that the additional calorie and protein allowances for pregnancy are applied for each fetus. [By using the figures from the 1948 *Dietary Standard for Canada* (18), which was in use when the Higgins method was formalized in 1963, in a twin pregnancy an additional daily intake of 4.2 MJ (1000 kcal) and 50 g protein is recommended after the 20th wk of gestation.]

The Higgins method was created at the Montreal Diet Dispensary to help compensate for the effect of the risk factors for adverse pregnancy outcome that are frequently observed in socially and economically disadvantaged women. These disadvantaged women receive priority for service at the Montreal Diet Dispensary and thus constitute the majority of women who are followed by dietitions who use the Higgins method each year. The dispensary's policy for service priority is different for twin pregnancies; all women regardless of socioeconomic status receive priority for service because of the greater medical risks these pregnancies involve. Service statistics indicate nonetheless that the majority of women with twin gestations who are followed by dietitions using the Higgins method at the Montreal Diet Dispensary are financially disadvantaged and tend to have the risks for adverse pregnancy outcome that are frequently observed among disadvantaged groups.

Study design

A review of medical charts was undertaken to determine differences in perinatal outcomes between two groups of twins. The intervention group consisted of twins born at 18 Montreal hospitals to mothers treated with the Higgins Nutrition Intervention Program at the Montreal Diet Dispensary between 1974 and 1988. The nonintervention group was a randomly selected subgroup of all twins born at the same hospitals as the intervention twins but known not to have been treated with the Higgins program. Because of the relative scarcity of twins treated with the Higgins program, a 2:1 sampling ratio of nonintervention to intervention twins was used. To control for confounding by possible differences in prenatal and obstetric care across hospitals as well as for changes in obstetric-management procedures that have occurred over time, this 2:1 sampling ratio was held constant within each hospital and within each year of birth for each hospital. The study was approved by an Ethics Committee of McGill University.

All data used in the present analyses were abstracted from the hospital medical charts; files maintained at the Montreal Diet Dispensary were used only to identify the intervention subjects. Reabstraction and recoding of the data from a random 3% of the medical charts in each hospital detected no systematic differences in abstraction or coding procedures between the two study archivists.

Data analysis

The unit for statistical analysis in this study was the individual twin infant rather than the average of twin pairs. This was done because although members of a twin pair may have been in utero at the same time, they may not have received exactly the same prenatal nutritional exposure because of physiological differences (eg, in placentation). In addition, twins can be discordant for the outcomes evaluated in this study; after birth, each member

TABLE 1
The Higgins method for classification and treatment of risks for adverse pregnancy outcome

Risk	Rehabilitation allowance
Undernutrition: Usual protein intake as determined by a diet history done at the initial assessment lower than the 1948 Canadian dietary standard recommendation*	Additional daily protein allowance set equal to assessed deficit in usual intake; 42 kJ (10 kcal) added for each gram of protein in rehabilitation allowance
Underweight: > 5% underweight†	Additional daily allowance of 20 g protein and 0.8 MJ (200 kcal) for each additional weekly 0.5 kg weight gain desired. Maximum possible additional gain set at 1.0 kg/wk‡
Stress condition: Poor outcome of prior pregnancy§, < 12 mo between birth of last infant and conception, failure to gain 5.0 kg by 20th week of pregnancy, pernicious vomiting (hyperemesis gravidarum), and serious emotional problems	Additional daily allowance of 10–20 g protein and 0.4–0.8 MJ (100–200 kcal) for each stress condition. Maximum total daily rehabilitation allowance for multiple conditions set at 40 g protein and 1.6 MJ (400 kcal)

* The 1948 *Dietary Standard for Canada* (18) was current when the Higgins Method was formalized in 1963; its figures have continued to be used since that time. The use of protein as a marker for the assessment of global nutrient adequacy in the Higgins intervention is based on the work of Jeans et al (19), which suggested that protein intake is predictive of the amount of other essential nutrients in the diet.

† Underweight was defined in comparison with desirable weights for adults prepared by the Metropolitan Life Insurance Company, 1959 (20).

‡ In 1972 the caloric portion of this rehabilitation allowance was changed from 0.8 MJ (200 kcal) to 2.0 MJ (500 kcal).

§ Poor outcome of prior pregnancy includes infants with birth weight < 2500 g, stillbirths, or spontaneous or therapeutic abortions.

of a twin pair receives care suited to a personal health profile and not necessarily to that of the twin.

Birth weight and the rates of low birth weight (< 2500 g), very-low birth weight (< 1500 g), preterm delivery (< 37 completed gestation weeks), very-preterm delivery (< 34 completed gestation weeks), and IUGR as well as perinatal morbidity and mortality were the outcome measures used. IUGR rates were based on intrauterine growth standards for singleton infants developed at the Royal Victoria Hospital (22).

Means and proportions were first used to describe the risk profiles and the pregnancy outcomes in the two treatment groups. Multivariable analyses (analysis of covariance and logistic regression) (23, 24) were then undertaken to compare pregnancy outcomes in these groups while controlling for the effect of six key confounding variables: socioeconomic status, pregravid weight, previous obstetrical history, smoking, underlying medical conditions known to affect pregnancy outcome (**Table 2**), and infant sex. Adjustment was made for previous obstetrical history because it contained information on two variables of interest: parity and previous poor obstetrical outcome (a risk for which there is a specific rehabilitation allowance in the Higgins method). Because the effect of these two variables cannot be studied independently, their combined effect was estimated by using the variable previous obstetrical history in a three-level form (no previous outcome, poor previous outcome, good previous outcome).

Because the assumption of equality of regression slopes in the two groups (ie, parallelism) was violated for three of the confounding variables (socioeconomic status, pregravid weight, and previous obstetrical history), their effects were estimated by using data from the nonintervention group alone. (It was not surprising that the assumption of equality of regression slopes was found to be violated for these variables; the Higgins intervention is designed specifically to prevent full expression of the effect of these risk factors for adverse pregnancy outcome.) The estimates of effect obtained from the nonintervention group for these three variables were used to adjust for their differing distributions in the two treatment groups before proceeding to classical analysis of covariance and logistic-regression techniques to adjust for the effects of unequal distributions of the other confounding variables (ie, smoking, underlying medical conditions known to affect pregnancy outcome, and infant sex). Because the final study groups were not completely balanced according to hospital and year of delivery, categorical variables representing these characteristics were also included in the analyses.

Calculation of the adjustment for the effect of pregravid weight by using data from the nonintervention group alone requires further description. In attempting to identify the model that best described the relationship between pregravid weight and birth weight, a cubic curvilinear model provided a better fit (ie, lowest mean square error, MSE) than either a linear or quadratic model. However, visual inspection of the data indicated that this curvilinear model was attempting to describe a relationship that was different below and above the pregravid weight of 50 kg. For this reason, as well as because 50 kg was one of two cutpoints used by the Committee to Study the Prevention of Low Birthweight (25) to define low pregravid weight in mothers with singleton pregnancies, different linear models were used to estimate the effect of pregravid weight on infant birth weight in the nonintervention group for pregravid weight < 50 kg and pregravid weight ≥ 50 kg. The improved fit of this piecewise linear model over that of a cubic curvilinear model was demonstrated by its lower MSE.

TABLE 2
Maternal profile

Characteristics	Intervention group (n = 177)	Nonintervention group (n = 343)
Age (y)	28 ± 5*	28 ± 4
Teenagers (%)	5	4
Nonwhite (%)	50	13†
Unmarried (%)	14	6†
Social assistance as source of income (%)	12	1†
Parity (%)	1.2 ± 1.4	0.7 ± 0.9†
Primiparas (%)	40	50†
Poor obstetrical history (%)‡	29	17†
Maternal height (cm)	163 ± 7	163 ± 7
Pregravid weight (kg)	60 ± 13	58 ± 10
Low pregravid weight, < 50 kg (%)	26	22
Smoked during pregnancy (%)	19	23
Underlying medical conditions (%)§	3	2

* $\bar{x} \pm$ SD.

† Significantly different from intervention group, $P \leq 0.05$.

‡ Any of the following: spontaneous abortion, fetal death, low-birth-weight infant.

§ Conditions known to affect perinatal outcomes: hypertension, renal disease, asthma, preexisting diabetes.

Two sets of subgroup analyses were also performed. The first set of analyses compared the outcomes for the intervention and nonintervention groups separately for infants of women with pregravid weights < and ≥ 50 kg. The second set of analyses separately compared the infants of the 132 mothers in the intervention group who had received a food supplement and the infants of the 45 mothers in the intervention group who had not received a food supplement with the infants of the mothers in the total nonintervention group. [Receipt of the food supplement as part of the intervention program requires a level of income comparable to that provided by social-assistance programs (21)]. This latter analysis was done because it provided a means for separately evaluating the impact of the intervention in these two potentially different groups followed by dietitions using the Higgins method. It is also seen as complementary to the overall analysis presented, which adjusted for the effect of differences in socioeconomic status in the two groups by using a variable constructed from data recorded in the medical charts. In that analysis, if there was data recorded in the medical charts indicating marital status as unmarried, source of income as social assistance, or maternal age at delivery as < 20 y, then socioeconomic status was coded as low; if none of these characteristics was recorded in the chart, socioeconomic status was coded as nonlow.

Odds ratios (OR) < 1 obtained from the logistic-regression analyses indicate a reduced risk of adverse outcome among the intervention infants. For example, an OR of 0.5 means that the odds of the intervention infants experiencing adverse outcomes is one-half that of nonintervention infants. Data were analyzed with *SYSTAT* Version 3 (26).

Results

A total of 189 mothers with twin gestations were enrolled in the Higgins program between 1974 and 1988. Eight of these

TABLE 3
Maternal progression of pregnancy

	Intervention group (*n* = 177)	Nonintervention group (*n* = 343)
Length of gestation (wk)	36.6 ± 3.0*	36.4 ± 3.1
Caesarean delivery (%)	51	48
Gestational weight gain (kg)	18 ± 7	16 ± 6†
Maternal morbidity (%)‡	30	42†
Pregnancy-induced hypertension (%)	12	15
Gestational diabetes (%)	4	6
Bleeding (%)§	10	16†
Premature rupture of membranes (%)	7	10
Hospitalization before 37 wk gestation (%)	62	67

* $\bar{x} \pm$ SD.
† Significantly different from intervention group, $P \leq 0.05$.
‡ Any of pregnancy-induced hypertension, gestational diabetes, bleeding, or premature rupture of membranes.
§ Includes placenta previa, abruptio placenta, and other antepartum bleeding.

women subsequently aborted one or both fetuses (< 500 g) and two women moved out of the province before delivery. In addition, the hospital charts of two women could not be traced when data abstraction was undertaken. The intervention group for this study thus consisted of 177 mothers (and their 354 twin infants) who had delivered at 18 Montreal-area hospitals. A total of 354 nonintervention mothers were frequency matched according to hospital and year of delivery to these 177 intervention mothers. Because 11 of the nonintervention mothers were noted to have been first admitted to other hospitals outside the Montreal area and then transferred to one of the 18 hospitals at which the intervention mothers had delivered, they were subsequently excluded from all analyses. This was done to avoid the possibility that a selection bias might have inflated the estimates of program impact obtained. The nonintervention group retained for these analyses thus consists of the remaining 343 (354 − 11) mothers and their 686 twin infants.

Descriptive data on characteristics of the study groups are presented in Table 2. Although the average age at delivery was the same in the two groups, there was a slightly higher proportion of teenagers in the intervention group. In addition, a higher proportion of the intervention group was nonwhite, was unmarried, and had social assistance indicated as source of income. The intervention group of mothers was of higher average parity but had more frequently experienced poor obstetrical outcomes in previous pregnancies. Pregravid weight in the intervention group averaged 2 kg higher than in the nonintervention group, but there was a slightly higher proportion of intervention women with a pregravid weight of < 50 kg. There was a slightly lower proportion of smokers in the intervention group. Because of the unequal distribution of these characteristics that could influence pregnancy outcome between the two treatment groups, all were initially included as confounding variables in the multivariable analyses presented below.

Descriptive data on maternal pregnancy outcomes are presented in Table 3. Duration of pregnancy was slightly longer in the intervention group than in the nonintervention group whereas gestational weight gain was 2 kg higher in the intervention group (18 kg) ($P < 0.05$). Caesarean deliveries occurred with equal frequencies in the two groups. Maternal morbidity was less frequent in the intervention group. The difference was statistically significant ($P < 0.05$) for the total group of variables constituting maternal morbidity as well as for antepartum bleeding. No maternal mortality was observed in this study.

Descriptive data on neonatal outcomes are presented in Tables 4 and 5. Because of the unequal distributions of potential confounding variables in the two groups, statistical tests of significance for differences in outcome were not performed at this stage of data analysis. It can be seen from Table 4 that the intervention infants appeared larger than the nonintervention infants in all dimensions: they weighed more, were longer, and had slightly greater head circumferences. Low birth weight, very-low birth weight, preterm delivery, and IUGR rates were lower in the intervention group; the rate of very-preterm delivery was slightly higher. As can be observed in Table 5, fetal mortality

TABLE 4
Descriptive data on neonatal outcomes

	Intervention group (*n* = 354)	Nonintervention group (*n* = 686)
Birth weight (g)	2468 ± 559*	2378 ± 620
Length (cm)	47.3 ± 4.3	46.7 ± 4.2
Head circumference (cm)	32.6 ± 2.8	32.3 ± 2.5
Males (%)	52	48
Combined placental weight (g)	978 ± 231	982 ± 244
Low birth weight (%)	47	55
Very-low birth weight (%)	5	9
Preterm (%)	40	47
Very preterm (%)	18	16
IUGR (%)†	14	18

* $\bar{x} \pm$ SD.
† Intrauterine growth retardation.

TABLE 5
Descriptive data on neonatal mortality and morbidity

	Intervention group (*n* = 354)	Nonintervention group (*n* = 686)
Fetal mortality (per 1000)	14	12
Early neonatal mortality (per 1000)	3	19
Transfer to another hospital (%)	1.7	4.4*
Neonatal intensive care (%)	49	53
Apgar score, 1 min	7.0 ± 2.2†	7.2 ± 2.1
Apgar score, 5 min	8.6 ± 1.6	8.6 ± 1.6
Infant morbidity (%)‡	8.5	10.6
Asphyxia (%)	1.7	1.2
Fractures and/or paralysis (%)	0.8	0.1
Respiratory-distress syndrome (%)	6.8	9.3
Malformations (%)	3.7	3.8

* Significantly different from intervention group, $P \leq 0.05$.
† $\bar{x} \pm$ SD.
‡ Any of asphyxia, fractures and/or paralysis, respiratory-distress syndrome.

(infants weighing ≥ 500 g born dead) was slightly higher but early neonatal mortality (infants weighing ≥ 500 g dying within the first week of life) was lower in the intervention than in the nonintervention group. This latter estimate may understate the true effect of the intervention. More nonintervention (4.4%) than intervention (1.7%) infants were transferred to other hospitals for care ($P < 0.05$); for these analyses all transferred infants were assumed to be alive. Apgar scores were essentially identical in the two groups. There was less respiratory-distress syndrome but more asphyxia and fractures in the intervention group. (All infants with fractures in the intervention group weighed < 2500 g.) Data on zygosity were seldom available in the medical charts. However, use of the Weinberg method [which uses data on numbers of like-sex and unlike-sex pairs to estimate the number of monozygotic (MZ) twins in any sample (27)] yielded similar estimates of the proportion of MZ twins in each treatment group.

Results of multivariable analyses comparing mean birth weight as well as rates of low birth weight, very-low birth weight, preterm delivery, very-preterm delivery, and IUGR while the effect of key confounding variables are controlled for are presented in **Table 6**. Although ORs for fetal and neonatal mortality are also presented in this table, these ratios have not been adjusted for the effect of confounders because of the small number of deaths that occurred in either group. After the effects of confounding variables are adjusted for, the birth weight of the intervention infants averaged 80 g higher ($P < 0.06$) than that of the nonintervention infants. The effect varied slightly across subgroups, with larger differences for infants of mothers with pregravid weights < 50 kg and for infants of intervention mothers who had not received the food supplement.

Except for fetal mortality, a pattern generally suggestive of lower risk (ie, OR < 1) for adverse pregnancy outcomes was observed in the intervention group (Table 6). Risk was significantly lower in the intervention group for low birth weight, very-low birth weight, and preterm delivery. The risk for early neonatal mortality was fivefold lower in the intervention group. [The lack of statistical significance ($P < 0.06$) may be at least partially related to the small numbers of deaths that occurred in either group.] Reductions in risk for adverse outcomes related to birth weight and length of gestation were more pronounced for the infants of mothers with pregravid weights < 50 kg than for those with pregravid weights ≥ 50 kg. No consistent pattern of differences between these groups was observed for mortality outcomes. In comparison with the nonintervention group, risks for adverse outcomes were generally reduced more substantially for the mothers in the intervention group who did not receive the food supplement than for mothers who did. The only exception was very-low birth weight, which occurred most frequently in the group of intervention mothers who did not receive the food supplement.

Race was included as a confounding variable in the initial stage of data analysis because race is associated with birth weight for singleton infants, and the percent of nonwhites was significantly higher in the intervention group. Univariable analyses, however, showed that differences in outcome associated with race were nonsignificant for the nonintervention group of twins

TABLE 6
Impact of the Higgins Nutrition Intervention Program on twin-pregnancy outcome

Risk categories	Birth weight of nonintervention infants	Birth-weight difference	Adjusted birth-weight difference*	Odds ratio for LBW*†	Odds ratio for VLBW*‡	Odds ratio for preterm delivery*	Odds ratio for very-preterm delivery*	Odds ratio for IUGR*	Odds ratio for fetal mortality	Odds ratio for early neonatal mortality
	g	*g*	*g*							
Overall	2378 ± 620§	90	80 ± 42‖	0.73¶ (0.54, 0.99)**	0.53¶ (0.29, 0.97)	0.68¶ (0.51, 0.92)	0.96 (0.64, 1.44)	0.94 (0.63, 1.41)	1.26 (0.43, 3.70)	0.21 (0.04, 1.15)
Subgroups defined by pregravid weight status										
Pregravid weight < 50 kg	2240 ± 567	93	88 ± 76	0.49¶ (0.26, 0.93)	0.55 (0.17, 1.78)	0.59 (0.32, 1.10)	0.79 (0.33, 1.90)	0.85 (0.41, 1.76)	0.50 (0.02, 12.41)	0.50 (0.02, 12.41)
Pregravid weight ≥ 50 kg	2416 ± 625	89	72 ± 50	0.84 (0.60, 1.19)	0.53 (0.26, 1.06)	0.72 (0.51, 1.00)	1.06 (0.67, 1.68)	0.94 (0.57, 1.55)	1.92 (0.58, 6.32)	0.29 (0.05, 1.66)
Subgroups defined by receipt of food supplement										
Receiving food supplement (n = 132)	2378 ± 620	50	60 ± 46	0.84 (0.60, 1.17)	0.41¶ (0.20, 0.84)	0.71¶ (0.52, 0.99)	1.05 (0.68, 1.63)	1.30 (0.83, 2.02)	1.69 (0.57, 4.99)	0.28 (0.05, 1.54)
Not receiving food supplement (n = 45)	2378 ± 620	206	115 ± 74	0.50¶ (0.30, 0.86)	1.21 (0.48, 3.04)	0.59¶ (0.35, 1.00)	0.75 (0.34, 1.65)	0.31¶ (0.12, 0.79)	0.44 (0.03, 7.71)	0.28 (0.02, 4.68)

* Adjusted for pregravid weight, socioeconomic status, previous obstetrical history, smoking, underlying medical conditions, infant sex, hospital, and year of delivery.
† LBW, low birth weight.
‡ VLBW, very-low birth weight.
§ $\bar{x}$ ± SD.
‖ $\bar{x}$ ± SEM.
¶ $P \leq 0.05$.
** Values in parentheses represent 95% confidence limits.

($P > 0.2$). In addition, in the multivariable analyses including other confounding variables, the effect of race on all outcome measures was highly insignificant ($P > 0.7$). For these reasons race was subsequently excluded from the multivariable analyses.

Adjustment for the effect of confounding variables decreased the difference in mean birth weight between the total study groups, increased the difference for the comparison involving infants of intervention women who had received the food supplement, and decreased the difference for the comparison involving intervention women who had not received the food supplement. The direction of these changes is consistent with the fact that visual inspection of the distributions of the confounding variables in the two groups (Table 2) suggest that the intervention group may have had somewhat lower biological risk but higher social risk for adverse birth outcomes.

Discussion

The goal of the Higgins Nutrition Intervention Program is to prevent adverse pregnancy outcomes through the treatment of pregnant women identified as at risk for those adverse outcomes. The effectiveness of this intervention for infants in singleton pregnancies was recently demonstrated (17). The results of the present study support the success of the Higgins program in improving the outcome of twin pregnancies as well.

After adjustment for differences in the distribution of key confounding variables, twin infants whose mothers were members of the intervention group weighed an average of 80 g ($P < 0.06$) more than did the nonintervention infants. Perhaps more importantly, associated with this mean adjusted increase of 80 g, the intervention infants had rates of low birth weight that were 25% lower ($P < 0.05$) and of very-low birth weight that were almost 50% lower ($P < 0.05$) than the rates observed for the nonintervention infants. Although these reductions compare favorably with those observed in evaluations of the impact of bed rest (3, 12), they were achieved with a nutrition intervention that is less costly and less likely to negatively influence family life than either hospital or at-home bed rest. The lower proportion of very-low-birth-weight infants in the intervention group in this study is seen as particularly important; the majority of infants in this birth-weight range are cared for in neonatal intensive-care units where costs are high (28–30).

Although the preterm delivery rate was 30% lower in the intervention group ($P < 0.05$), rates of IUGR were similar in the two groups. This is not the first time that nutrition supplementation was observed to affect birth weight through length of gestation rather than the rate of growth in utero. In an evaluation of the Guatemalan longitudinal study of nutrition supplementation during pregnancy, Villar et al (31) reported that calorie and/or protein supplementation lowered the incidence of preterm delivery by 50% but did not affect the incidence of IUGR. More specific to this study, however, it is also possible that the longer length of gestation in the intervention group partially masked an effect of the intervention on IUGR; the IUGR rate appears to increase for twins as pregnancy approaches term (8, 9). The possibility should also be considered that differences in rates of IUGR were not observed because the growth standards used (22) are based on singleton births, and their values may be too high to identify twins who are growth retarded in relation to other twins.

There was little difference in IUGR rates in the intervention and nonintervention groups. Note, however, that although the intervention group receiving the food supplement had a slightly greater risk for IUGR than did the nonintervention group (OR = 1.30, NS), the intervention group not receiving the food supplement had a significantly lower risk (OR = 0.31, $P < 0.05$). It is thus possible that underlying risk factors associated with poverty (and perhaps long-term malnutrition) may have produced a substantially higher baseline risk for IUGR for the members of the intervention group who received the food supplement and that the Higgins intervention was not able to completely prevent its expression.

A different baseline risk may also partially explain the slightly higher fetal mortality in the intervention group. All excess fetal mortality occurred among members of the intervention group who required the food supplement for reasons of financial need. This group also had the highest risk of IUGR, a condition reported by several authors to be associated with fetal mortality (4, 14, 32). Neonatal mortality, on the other hand, was almost fivefold lower for the intervention infants ($P < 0.06$). Reasons for this difference may be related to the fact that preterm delivery was significantly lower in the intervention group and neonatal mortality occurs more frequently for preterm infants (12, 14, 32).

No detailed dietary intake information was available for the nonintervention group. However, given the unique nature of the Higgins program for multiple gestations [ie, mothers are taught to consume an extra 2.1 MJ (500 kcal) and 25 g protein to cover the needs of each fetus after 20 wk gestation], the intervention women would have been expected to have had, on average, a greater food intake during pregnancy. Indirect confirmation of higher food consumption in the intervention group is provided by the fact that despite their slightly higher pregravid weights these women gained an average of 2 kg more than did the nonintervention group: 18 vs 16 kg ($P < 0.05$). There was, however, less pregnancy-induced hypertension and less gestational diabetes in the intervention group. In addition, the weight gain in both groups was similar to the gain of 18.5 kg observed in a study of 217 women delivering twins in a large urban hospital serving a largely middle-class population (33).

There is a specific rehabilitation allowance in the Higgins program to reduce the impact of low pregravid weight on pregnancy outcome. Its success in achieving this goal is attested to by the fact that for all outcome measures except early neonatal mortality the reduction in adverse outcomes associated with the intervention was greater for infants born to mothers with pregravid weights < 50 kg than for those whose mothers had higher pregravid weights (Table 6). Given that these mothers are easily identifiable, they form an ideal group for selective intervention if a nutrition-intervention program must be introduced gradually.

For all outcome measures except very-low birth weight, the reduction in risk for adverse pregnancy outcome associated with the intervention was less for the intervention subgroup receiving the food supplement for reasons of financial need than for the intervention subgroup not receiving the food supplement (Table 6). It is possible that the smaller impact in the former group is related to the fact that the women who received the food supplement may have had a greater than average baseline risk for adverse pregnancy outcome. Support for such an explicative mechanism is provided in the literature on singleton pregnancies. Infants born to socially and economically disadvantaged women generally weigh 200–300 g less at birth than do those born to nondisadvantaged women, and their low-birth-weight rate is almost twice as high (25, 34, 35).

In summary, the findings of this study demonstrate the effectiveness of the Higgins Nutrition Intervention Program in generally improving the outcome of twin pregnancies. Given that very-low-birth-weight infants are most frequently cared for in neonatal intensive-care units, the reduction in risk for this outcome measure is seen as particularly important.

References

1. DeMuylder X, Moutquin JM, Desgranges MF, Leduc B, Lazaro-Lopez F. Obstetrical profile of twin pregnancies: a retrospective review of 11 years (1969–1979) at Hôpital Notre-Dame, Montréal, Canada. Acta Genet Med Gemellol (Roma) 1982;31:149–55.
2. Grothe W, Rüttgers H. Twin pregnancies: an 11 year review. Acta Genet Med Gemellol (Roma) 1985;34:49–58.
3. Hays PM, Smeltzer JS. Multiple gestation. Clin Obstet Gynecol 1986;29:264–85.
4. Manlan G, Scott KE. Contribution of twin pregnancy to perinatal mortality and fetal growth retardation; reversal of growth retardation after birth. Can Med Assoc J 1978;118:365–8.
5. Fabia J. Perinatal mortality in Québec II twins. Vie Med Can Fr 1979;8:28–35 (in French).
6. Ghai V, Vidyasagar D. Morbidity and mortality in twins. An epidemiologic approach. Clin Perinatol 1988:15:123–39.
7. Jones JM, Sbarra AJ, CL Cetrulo. Antepartum management of twin gestation. Clin Obstet Gynecol 1990;33:32–41.
8. Bleker OP, Kloosterman GJ, Huidekoper BL, Breur W. Intrauterine growth of twins as estimated from birth weight and fetal biparietal parameter. Eur J Obstet Gynecol Reprod Biol 1977;7:85–90.
9. Fliegner JR, Eggers TR. The relationship between gestational age and birth-weight in twin pregnancy. Aust N Z J Obstet Gynaecol 1984;24:192–7.
10. Pritchard JA, MacDonald PC, Grant NF. Williams obstetrics. Norwalk, CT: Appleton-Century-Crofts, 1985.
11. Cetrulo CL, Ingardia CJ, Sbarra AJ. Management of multiple gestation. Clin Obstet Gynecol 1980;23:533–48.
12. Newton ER. Antepartum care in multiple gestation. Semin Perinatol 1986;10:19–29.
13. Clarkson JE, Buckfield PM, Herbison. The outcome of twin pregnancies in Dunedin 1968–1978. Aust N Z J Obstet Gynaecol 1982:22:127–30.
14. Ahn MO, Phelan JP. Multiple pregnancy: antepartum management. Clin Perinatol 1988;15:55–69.
15. Yeast JD. Maternal physiologic adaptation to twin gestation. Clin Obstet Gynecol 1990;33:10–7.
16. Campbell DM, MacGillvray I, Tuttle S. Maternal nutrition in twin pregnancy. Acta Genet Med Gemellol (Roma) 1982:32:221–7.
17. Higgins AC, Moxley JE, Pencharz PB, Mikolainis D, Dubois S. Impact of the Higgins Nutrition Intervention Program on birthweight: results of a within-mother analysis. J Am Diet Assoc 1989:89:1097–103.
18. Canadian Council on Nutrition. Dietary standard for Canada. Ottawa: Department of Public Printing and Stationery, 1950.
19. Jeans PC, Smith MB, Stearns G. Incidence of prematurity in relation to maternal nutrition. J Am Diet Assoc 1955;31:576–81.
20. Metropolitan Life Insurance Company. 1960 New weight standards for men and women. Stat Bull Metropol Life Insur Co 1959; 40:1–4.
21. Montreal Diet Dispensary. Budgeting for basic needs and budgeting minimum adequate standard of living. Montreal: Montreal Diet Dispensary, 1974–1988.
22. Usher RH, McLean F. Intrauterine growth of liveborn Caucasian infants at sea level: standards obtained from measurements in seven dimensions of infants born between 25 and 44 weeks of gestation. J Pediatr 1969;74:901–10.
23. Anderson S, Auquier A, Hauck WW, Oakes D, Vandaele W, Weisberg HI. Statistical methods for comparative studies. Techniques for bias reduction. New York: John Wiley & Sons. 1980.
24. Fleiss JL. Statistical methods for rates and proportions. New York: John Wiley & Sons, 1981.
25. Institute of Medicine. Preventing low birth weight. Washington, DC: National Academy Press, 1985.
26. Wilkinson L. SYSTAT: the system for statistics. Version 3. Evanston, IL: SYSTAT Inc, 1987.
27. Nylander PPS. The phenomenon of twinning. In: Barron SL, Thomson AM eds. Obstetrical epidemiology. London: Academic Press, 1983:146–7.
28. Boyle MH, Torrance GW, Sinclair JC, Horwood SP. Economic evaluation of neonatal intensive care of very-low-birth-weight infants. N Engl J Med 1983;308:1330–7.
29. Sandu B, Stevenson RC, Cooke RWI, Pharoah POD. Cost of neonatal intensive care for very-low-birth weight infants. Lancet. 1986;1: 600–3.
30. Mugford M. A review of the economics of care for sick newborn infants. Community Med 1988;10:99–111.
31. Villar J, Khoury MJ, Finucane FF, Delgado HL. Differences in the epidemiology of prematurity and intrauterine growth retardation. Early Hum Dev 1986;14:307–20.
32. Desgranges MF, Muylder X, Moutquin JM, Lazaro-Lopez F, Leduc B. Perinatal profile of twin pregnancies: a retrospective review of 11 years (1969–1979) at Hôpital Notre-Dame, Montréal, Canada. Acta Genet Med Gemellol (Roma) 1982;31:157–63.
33. Pederson AL, Worthington-Roberts B, Hickok DE. Weight gain patterns during twin gestation. J Am Diet Assoc 1989;89:642–6.
34. Saugstad LF. Weight of all births and infant mortality. J Epidemiol Community Health 1981;35:185–91.
35. Pelchat Y, Wilkins R. Birth data: some socio-demographic and health characteristics of mothers and their newborns in region 6A (metropolitain Montréal), 1979–1983. Montréal: Regroupement des départements de santé communautaire du Montréal-Métropolitain, 1987 (in French).