Acta Genet Med Gemellol 44-2: 93-101 (1995)

Prenatal Weight Gain and the Birthweight of Triplets

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Abstract. The objective of this study was to evaluate the association between maternal factors, including rates of gestational weight gain before and after 24 weeks' gestation, and adequacy of intrauterine growth for gestational age at birth of triplets, as a mean Z-score of the triplet set. The study design was a retrospective, anonymous, pilot telephone survey of mothers of triplets and an historical cohort analysis of their prenatal weight gain records. The statistical analyses performed included multiple regression analysis to formulate a model for mean triplet Z-score (a measure of birthweight-for-gestational age) and analysis of variance to confirm and simplify the components of this model. Factors significant in the final model and their beta coefficients included weeks' gestation (−0.124, $p < 0.0001$), rate of gain before 24 weeks' gestation (0.606, $p = 0.005$), and induced conception (−0.404, $p = 0.01$). Rate of gain ≥ 1.5 lbs/week before 24 weeks was significant in the analysis of variance ($p = 0.009$). Better intrauterine growth for gestational age is achieved in triplet gestations with maternal weight gains of ≥ 1.5 lbs/week before 24 weeks' gestation.

Key words: Triplet birthweight, Maternal weight gain

INTRODUCTION

During recent years, the number of multiple births in many countries has risen dramatically [15]. In the United States, for example, between 1972 and 1992 the number of singleton births increased by 24%, while twin births increased by 61% and triplet and higher order births increased by 328% [26, 27]. In absolute numbers, twin births increased from 59,122 to 95,372 and triplet and higher order births from 907 to 3,883 during this 20-year period [26, 27].

This trend is due to several factors. Because of the rapid rise in the birth rate in the 1950s, followed by a decline in the 1960s and 1970s, the largest cohort of women of reproductive age in the 1990s are over 30 years of age. The incidence of multiple births occurs with greater natural frequency among older women. In addition, more women in the United States are choosing to delay childbearing for financial, educational, and career reasons. For example, in the United States between 1972 and 1992, the proportion of first and of all infants born to women age 30 and older increased from 4% to 20% and from 17% to 32% respectively [26, 27]. Infertility is also higher among women in this age group. Data from the British Study of Triplet and Higher Order Births estimated an odds ratio (OR) of 31.2 (95% confidence interval (CI), 12.5-99.7) of having a triplet birth associated with the use of drug therapy for infertility [4]. As a result of these factors, higher maternal age and fertility-enhancing agents, the incidence of multiple births has increased during recent years.

In the United States in 1992, live births of triplet and higher order multiple births accounted for 0.1% of all live births, live births of twins for 2.3% and live births of singletons for 97.6% [27]. Despite being a small proportion of total births, multiples are over-represented among low birthweight (LBW, <2500 g) and very low birthweight (VLBW, <1500 g) infants. For example, more than 90% of triplets weigh less than 2500 g at birth, compared to 50% of twins and 6% of singletons. And more than 33% of triplets weigh less than 1500 g at birth compared to 10% of twins and 1% of singletons. As a result of this skewed birthweight distribution, in combination with a skewed gestational age distribution, infants of multiple gestation subsequently experience a disproportionate amount of morbidity and mortality compared to singletons. The relative risk of neonatal death compared to singletons is 7.2 for twins and 21.6 for triplets, while that for postneonatal death is 3.1 for twins and 6.4 for triplets [16]. Among survivors, the relative risk of severe handicap compared to singletons is 1.7 for twins and 2.9 for triplets [16].

Maternal weight gain in singleton pregnancy is strongly associated with higher birthweights [12, 25]. Although less research has been conducted in multiple gestations, several studies have shown an association between maternal weight gain and twin birthweight [5, 14, 17, 18, 22]. A national report published a few years ago in the United States, recommended a 35-45 lbs weight gain for a term, twin pregnancy [12]. There is much less data and there are currently no recommendations on maternal weight gain in triplet pregnancies. When weight gain data has been reported, it has usually been from case reports and frequently does not consider the factors of maternal pregravid weight, parity, or the pattern of weight gain [9, 24]. Studies of singleton [1, 11, 23] and twin [17, 18, 22] pregnancies indicate that the pattern of weight gain may be as important as total weight gain. In singleton gestations, inadequate early rate of gain (<9.5 lbs by 24 weeks' gestation) is associated with an increased risk of low birthweight for gestational age, whereas inadequate late rate of gain (<0.9 lbs/week after 24 weeks' gestation) or an overall low rate of gain (<0.6 lbs/week) is associated with a significant increase in preterm delivery [1, 11, 23]. In twin gestations, higher early rate of gain (≥ 24 lbs by 24 weeks' gestation) and higher late rate of gain (≥ 1.5 lbs/week after 24 weeks' gestation) are each associated with better birthweights [18, 22]. Current therapies used in triplet pregnancies to improve birthweight or prolong gestation, such as routine hospitalization [7, 21] and prophylactic tocolysis [21] have not proven to be consistently effective. Enhanced maternal weight gain, particularly before 24 weeks' gestation, may be an important therapeutic method of improving triplet birthweight and perinatal outcome. The purpose of this pilot study is to evaluate the association between maternal factors, particularly pregravid weight, weight gain, and rates of weight gain before and after 24 weeks' gestation, and triplet birthweight and adequacy of intrauterine growth for gestational age.

MATERIALS AND METHODS

The population for this pilot study was chosen from women who had brought their triplet children to the Multiple Births Foundation Clinic in London, United Kingdom, and who had given birth since 1983. Demographic, anthropometric, and perinatal data was collected by telephone interview by a research nurse. This data included maternal age at delivery, method of conception (induced vs natural), height and pregravid weight, parity, smoking habits, length of gestation, and the triplets' birthweights. In the United Kingdom, pertinent information is noted in the medical record during each prenatal visit, but this special record, called a Cooperation Card, is retained by the patient herself during and after the pregnancy. It was possible, therefore, to obtain information regarding prenatal weights and dates from the Cooperation Cards of each mother during the telephone interview.

The study sample was limited to triplet pregnancies meeting the following inclusion criteria: complete data available on height, pregravid weight, last menstrual period or expected date of delivery and actual date of delivery, and Cooperation Card data available on prenatal dates and weights including prenatal weight at 24 weeks' gestation or at 23 and 25 weeks' gestation, last recorded weight within one week of delivery, and birthweights of all three liveborn triplets.

The independent variables in the present study were maternal age at delivery, method of conception, pregravid body mass index (BMI, or weight/height^2), parity (primipara vs multipara), smoking before or during pregnancy, total weight gain, early rate of weight gain (before 24 weeks' gestation), and late rate of weight gain (after 24 weeks' gestation to delivery). The BMI was modelled as both a continuous variable and as a categorical variable (underweight, <19.8; normal weight, 19.8-26.0; or overweight, >26.0), according to the most recent American guidelines [12]. Length of gestation was also modelled as both continuous and categorical variables (as the clinically relevant categories of 27-30 weeks, 31-34 weeks, or 35-37 weeks). Weight gain was modelled as total weight gain, early rate of gain, and late rate of gain. Total weight gain was based on the difference between the last prenatal weight before delivery and the pregravid weight. Early rate of gain was calculated as the difference between maternal pregravid weight and weight at 24 weeks' gestation, and, divided by 24 weeks, on the basis of prenatal weights taken at 24 weeks or interpolated on the basis of weights measured within one week before or after this date [1, 23]. Late rate of gain was calculated as the difference between maternal prenatal weight at 24 weeks' gestation and the delivery weight, divided by the difference in weeks' gestation.

The dependent variable in this study was mean birthweight for gestational age, as a Z-score. For descriptive purposes, birthweight was also calculated as the total birthweight (the sum of each triplet set) and as the mean birthweight (mean of the triplet set). The Z-score of the triplet set was based on the mean birthweight. The Z-score represents the distance of the observed value from the median of the age-and gender-specific reference curve, expressed in standard deviation (SD) units [8]. For example, a Z-score of −1.2 or less is 1.2 SD from the median and is equivalent to about the 10th percentile; a Z-score of −2.0 represents a measurement 2 SD from the median, equivalent to about the 2nd percentile. Gestational age- and gender-specific standards from the Centers for Disease Control were used to calculate the Z-scores. This study was approved by both the Committee on Research at the Queen Charlotte's and Chelsea Hospital, London, United Kingdom, where the study was conducted, and the Human Investigation Committee at the Rush-Presbyterian-St. Luke's Medical Center in Chicago, where the study was designed and analyzed.

The data was analyzed using SPSS 5.0 statistical software [Version 5.0 for the IBM PC/XT/AT and PS/2, Chicago, Il, 1993]. First, descriptive statistics of the study sample were generated, including means and standard deviations (SD) for continuous data and percentages for categorical data. Next, study variables were compared across gestational categories and according to whether the pregnancy was the result of an induced or a natural conception. Because of the small sample size, nonparametric methods were used, including the Fishers exact chi-square test for proportions, the Kolmogorov-Smirnov two-sample test for continuous variables and the Kruskal-Wallis one-way analysis of variance for continuous variables for three groups. With mean Z-score as the dependent variable, multiple stepwise regression analysis was then used to formulate a model, and analysis of variance used to confirm and simplify the components of the model.

RESULTS

A total of 38 triplet pregnancies were included in the study population, with delivery dates ranging from 1983 to 1993; 87% (33/38) had delivered between 1988 and 1993. A description of the total study population and by gestation categories is given in Table 1. The mean maternal age was more than 30 years, about 70% of mothers were primiparas, and more than 70% of the triplet pregnancies were the result of induced conceptions. The mean gestational age was 33.4 weeks, with nearly two-thirds of all births occurring before 35 weeks' gestation. Mean gestational weight gain was about 44 lbs; mean triplet birthweight was 1805 g and mean Z-score was −1.14.

When stratified by gestation categories, several differences became apparent. Although mean birthweight parallelled increasing gestation, the mean Z-score dropped dramatically at 35-37 weeks. The proportion of Z-scores <-1.2 was 4-5 times higher and the proportion <-2.0 was twice as high at 35-37 weeks compared to the earlier gestation categories. Women who gave birth at 31-34 weeks were more likely to be of normal weight, gain more total weight, have a higher rate of gain after 24 weeks, and were more likely to have a rate of gain before 24 weeks of ≥ 1.5 lbs/week. Women who gave birth at 35-37 weeks were more likely to have had an induced conception and to have been underweight pregravid. These data are shown in Table 1.

Table 1 - Description of total study population and by gestation categories

Variable		Gestation categories				
		Total	27-30 Weeks	31-34 Weeks	35-37 Weeks	P Value
N	(mothers)	38	7	17	14	
	(infants)	114	21	51	42	
Maternal	age (years)	30.7±4.0	28.1±4.0	31.4±3.8	31.1±4.0	*
	height (inches)	64.6±2.7	63.9±2.3	64.5±2.4	65.5±3.2	*
	pregravid weight (lbs)	128.6±16.7	128.4±18.0	127.5±14.3	129.6±19.8	*
Body mass index (BMI)		21.5±2.3	22.0±3.2	21.4±1.7	21.4±2.6	*
% underweight (BMI <19.8)		23.7%	14.3%	17.6%	35.7%	*
% normal weight (BMI 19.8-26.0)		71.1%	71.4%	82.4%	57.1%	*
% overweight (BMI >26.0)		5.2%	14.3%	0%	7.1%	*
% Smoking before pregnancy		13.2%	14.3%	17.6%	7.1%	*
% Primiparas		71.1%	71.4%	76.5%	64.3%	*
% Induced conception		71.1%	71.4%	58.8%	85.7%	*
Weeks gestation (mean)		33.4±2.6	29.0±1.0	33.2±1.2	35.9±0.8	<0.0001
Total gestational weight gain (lbs)		43.9±15.5	39.4±13.6	48.3±15.7	40.2±15.6	*
Rate of gestional weight gain/week						
before 24 weeks		1.06±0.4	1.13±0.2	1.10±0.5	0.97±0.3	*
after 24 weeks		2.12±1.2	1.69±0.6	2.38±1.4	1.99±1.2	*
before 24 weeks ≥1.5lb/week (%)		11.4%	0%	18.8%	7.7%	*
Birthweight sum of triplet set (g)		5415±1229	3452±485	5424±682	6385±728	<0.0001
Mean of triplet set (g)		1805±410	1150±162	1808±227	2128±243	<0.0001
Mean Z-score**		-1.14±0.7	-0.89±.81	-0.85±.56	-1.63±.59	0.001
% Z-scores <-1.2		31.6%	14.3%	11.8%	64.3%	0.004
% Z-scores <-2.0		13.2%	14.3%	0%	28.6%	0.05

Note: Values are given as mean ± Standard Deviation (SD) for numerical variables and percent (%) frequency for categorical variables.

* is not statistically significant, p<.05, two-tailed.

** Z-score equals the observed value minus the reference mean value, divided by the reference SD value. Across gestation categories, continuous variables were compared by the Kruskal-Wallis one-way analysis of variance and frequencies by Fisher's exact test.

Women with induced conceptions were significantly older than their natural counterparts (32.0±3.6 vs 27.6±3.2 years, p<0.5), and also tended to be thinner (29.6% underweight vs 9.1%), smoke before conception (18.5% vs 0%), gain less during pregnancy (40.6±13.1 lbs vs 50.7±18.4 lbs), and have longer gestations (33.6±2.7 weeks vs 32.9±2.6 weeks). While not statistically significant, a higher proportion of infants of induced triplet pregnancies were moderately growth-retarded (Z-scores <-1.2, 37% vs 18.2%) or severely growth-retarded (Z-scores <-2.0, 18.5% vs 0%).

The final multiple regression model for mean Z-scores included three factors and resulted in a multiple R of 0.785, and R^2 of 0.615. The multiple R indicates the degree of association between the dependent variable and the independent variables in the final model, and the R^2 indicates the extent to which the variance in the dependent variable was explained by the independent variables in the final model. The significance of the regression was demonstrated by the F statistic, at 14.41, $p<0.00001$. Weeks' gestation and induced conception both had negative coefficients in the final model; rate of gain before 24 weeks' gestation was the only positive coefficient. Table 2 summarizes the multiple regression model and the beta coefficients.

Table 2 - Summary of multiple regression model

Dependent variable	Final model	Beta coefficient	SE Beta coefficient	Significance
Mean triplet Z-score	Weeks gestation	−0.124	0.027	0.0001
Multiple R: 0.785	Rate of gain before 24 weeks	0.606	0.201	0.005
R^2: 0.615	Induced conception	−0.404	0.153	0.01
F value: 14.41				
P value: <0.00001				

Using the three factors significant in the multiple regression model as categorical variables, three-way analysis of variance was then performed. Method of conception was classified as natural vs induced (0 vs 1), gestation as 27-30 weeks, 31-34 weeks, or 35-37 weeks; rate of weight gain before 24 weeks' gestation as <1.5 lbs/week or ≥1.5 lbs/week, based on prior case reports [10]. The main effects of method, gestation category, and rate of gain before 24 weeks' gestation were all significant. Second- and higher-order interactions were not considered because of the small sample size. Table 3 summarizes the analysis of variance results.

Table 3 - Analysis of variance results

Dependent variable	Independent variable	F ratio	Significance
Mean triplet Z-score	Main effects	8.78	<0.0001
	Induced conception	4.46	0.04
	Gestation category	8.95	0.001
	Rate of gain before 24 weeks ≥1.5 lb/week	7.91	0.009

DISCUSSION

The results of this study indicate that the adequacy of intrauterine growth for gestational age, as measured by the Z-Score, is significantly influenced by method of conception, weeks gestation, and rate of maternal weight gain before 24 weeks' gestation. The Z-score was chosen because it is a better measure of the adequacy of growth for gestational age than birthweight alone. In other studies of twin pregnancies, growth retardation (as a Z-score, <-1.2) was significantly associated with increases in both morbidity [20] and mortality [19].

These findings confirm those of earlier triplet studies, that maternal weight gain plays an important role in prenatal growth. The mean maternal weight gain in this study of 38 triplet pregnancies was 43.9 lbs in 33.4 weeks, which was comparable to the findings of the 1138 triplet pregnancies studied by one group of researchers of 45.1 lbs in 33.8 weeks [9]. On the basis of Pearson (R) correlation coefficients, this group demonstrated a strong, significant association between maternal weight gain and triplet birthweight. Multiple regression analysis in this study showed rate of weight gain before 24 weeks' gestation to have a significant association with mean birthweight for gestational age, expressed as a Z-score.

The pattern of maternal weight gain may partially reflect the accretion and utilization of maternal body fat, a process modulated by the hormonal environment. Body fat is a significant extragonadal source of estrogen and a storage site for steroid hormones. The accretion of body fat during pregnancy, as reflected in the early rate of weight gain, may influence the complex hormonal mechanisms mediating intrauterine growth. In singleton pregnancies, the relationship between poor patterns of weight gain before 24 weeks' gestation [11] or between 28 and 32 weeks' gestation [13] may be an indirect reflection of the hormonal role of maternal body fat on birthweight. The accretion and utilization of body fat correlated with better singleton birthweights and longer gestations [2, 3]. As a dichotomous variable in the analysis of variance, maternal weight gain of ≥ 1.5 lbs/week before 24 weeks' gestation (≥ 36 lbs by 24 weeks) was associated with significantly higher mean Z-scores ($p = 0.009$). This rate of gain was achieved by only 11.4% of women in this study.

The results of this study also suggest that the optimal combination of birthweight and gestation for triplets may differ from that for twins and certainly from that for singletons. In twin gestations, because of accelerated lung maturation and ageing of the placenta, the optimal combination associated with the lowest morbidity and mortality is 2500-2800 g at 35-38 weeks' gestation, about 1000 g less and three weeks earlier than for singletons [18, 19]. This ideal combination has yet to be defined for triplet gestations, but the data from this study suggest that the maturity achieved by 35-37 weeks' gestation is at the expense of substantial growth retardation, and with consequences for morbidity and mortality. The limitations of the present study include the small sample size (38 triplet pregnancies and 114 triplet infants), the lack of racial and socioeconomic diversity, and missing information regarding prenatal and postnatal complications. Despite these limitations, this study adds important clinical information to the growing body of obstetric literature regarding the importance of maternal nutrition in these high-risk pregnancies. Ideally, a prospective maternal nutrition study of triplet gestations should be conducted, with serial measurements of maternal body fat, hormonal assessments, and tests of placental function, size, and structure.

Acknowlegement: This study was supported by funding from the Center for the Study of Multiple Births, Chicago, Illinois.

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