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Influence of Clinical Variables on Triplet Birth Weight

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Abstract. The small size of most reported triplet series has resulted in conflicting statements about the influence of several clinical variables on triplet birth weight. Therefore, obstetrical and neonatal data were collected on 196 mothers and their 580 infants (8 stillbirths excluded). Gestational age was based on the date of fertilization in 13 IVF triplets and on the date of ovulation in 90 medically induced triplets. Obstetrical and ultrasonic criteria were used to estimate the date of confinement in 93 spontaneous triplets. Birth weight appeared to be higher in males and with higher maternal parity, independent of gestational age. The apparent effect of medical technologies such as ovulation induction or IVF on combined triplet birth weight disappeared when maternal parity and fetal gender were controlled. Preeclampsia, maternal race and zygosity were not significantly associated with birth weight. While birth order did not significantly effect ultimate birth weight, the heaviest triplet did present first more often than would be expected by chance alone. Future evaluation of neonatal outcome data in multifetal gestations should control for gestational age, fetal gender and maternal parity. It appears that triplet birth weight is not affected by etiology, which is important given the significant impact of medical technologies.

Key words: Triplets, Birth weight, Fetal gender, Parity, Birth order

INTRODUCTION

Due to the small size of most reported triplet series, there have arisen several conflicting statements in the literature regarding the influence of various maternal and fetal variables on triplet birth weight. The following study examined a large series of triplet gestations delivered between 1985 and 1988 to help resolve some of these controversies. Maternal demographic factors, antepartum complications, and triplet variables were assessed for their impact on combined and individual triplet birth weights and gestational

age at delivery. Of specific interest is the impact of medical technologies such as ovulation induction and in vitro fertilization (IVF) on triplet birth weight given the ever expanding role of these technologies on the frequency of triplet birth.

MATERIALS AND METHODS

Obstetrical and neonatal data were collected on 196 mothers and their 580 infants (8 stillbirths excluded). Data were collected with the assistance of ambulatory perinatal nurses employed by the Tokos Medical Corporation. The perinatal nurses were in daily contact with these women for the purpose of antepartum surveillance for preterm-birth prevention beginning at an average gestational age of 23.8 ± 3.3 weeks' gestation. Data were recorded on daily obstetrical care records maintained by the perinatal nurses from the time of referral through delivery.

Gestational age was based on the date of fertilization in 13 IVF triplets and on the date of ovulation in 90 medically induced triplets. Early obstetrical and ultrasonic criteria were used to estimate the date of confinement and gestational age in 93 spontaneous triplets. All triplet gestations were known at the time of their referral for ambulatory surveillance. During the 3-year study period, from 1985 to 1988, there was an even distribution of the IVF and medically induced triplets. The specific determination of zygosity was not available. Zygosity was approximated by assuming all monozygotic triplets would be included among the same-sex spontaneous triplets and dizygotic or trizygotic triplets would be represented by the mixed-sex spontaneous triplets, the induced ovulation triplets, and the IVF triplets.

Preterm labor was defined as the presence of regular uterine contractions associated with progressive cervical dilatation and/or effacement prior to 37 completed weeks' gestation. Preeclampsia was diagnosed clinically by the attending obstetrician based on the presence of pregnancy-induced hypertension, proteinuria, and edema.

Data are presented as means ± standard deviation (X ± SD). Statistical evaluation included the one-way and three-way analysis of variance, the correlation coefficient, and the chi-square test. Statistical comparisons were performed using the Minitab and the BMDP statistical packages.

RESULTS

The mean birth weight for each individual triplet was 1864 ± 543 g and 5593 ± 1488 g for each triplet set. The mean gestational age at delivery for the entire triplet series was 33.6 ± 3.1 weeks.

Maternal age was correlated with both the combined birth weight and gestational age at delivery for each triplet set. The correlation coefficients for maternal age with birth weight ($R = 0.032$) and gestational age ($R = 0.012$) were both nonsignificant. The correlation between combined birth weight and gestational age, however, was highly significant ($R = 0.85$). The effects of maternal race, parity and etiology on combined triplet birth weight and gestational age were evaluated using the one-way analysis of variance and are presented in Table 1.

Table 1 - Maternal demographic factors affecting triple birth weight and gestational age

Factor	N	Birth weight (g)	Gestational age (wk)
Race			
White	158	5576 ± 1492	33.4 ± 3.2
Black	30	5921 ± 1373	34.7 ± 2.5
Other	8	5551 ± 1421	32.6 ± 2.8
		p = 0.51	p = 0.07
Parity			
Nulliparous	101	5322 ± 1322	33.1 ± 3.1
Primipara	66	5904 ± 1586	34.2 ± 3.0
Parity ≥ 2	29	6004 ±1490	33.7 ± 3.2
		p = 0.015*	p = 0.11
Etiology			
Spontaneous	93	5842 ± 1597	33.0 ± 3.1
Induced	90	5342 ± 1655	34.1 ± 3.2
IVF	13	5455 ± 1454	33.8 ± 2.2
		p = 0.014*	p = 0.043*

Two major antepartum complications which may affect combined triplet birth weight are preeclampsia and preterm labor. The effects of these complications on triplet outcome were also evaluated using the one-way analysis of variance and are presented in Table 2.

Table 2 - *Antepartum complications affecting triplet birth weight and gestational age*

Factor	N	Birth weight (g)	Gestational age (wk)
Preeclampsia			
Yes	30	5368 ± 1082	33.5 ± 2.0
No	166	5703 ± 1559	33.6 ± 3.3
		p = 0.18	p = 0.51
Preterm labor			
Yes	123	5191 ± 1372	32.5 ± 3.0
No	73	6402 ± 1392	35.4 ± 2.3
		p = 0.0001*	p = 0.001*

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Fetal characteristics evaluated for their possible influence on either birth weight or gestational age include fetal gender, birth order, and zygosity. Again, these factors were evaluated using the one-way analysis of variance and are presented in Table 3. While birth order failed to have any significant effect on triplet birth weight, the heaviest infant did present first with a greater frequency than expected by chance alone ($p = 0.001$, χ^2 test).

Table 3 - Triplet characteristics affecting birth weight and gestational age

Factor	N	Birth weight (g)	Gestational age (wk)
Fetal sex			
Male	227	1959 ± 548	33.6 ± 3.1
Female	303	1790 ± 535	33.5 ± 3.1
		p = 0.0001*	p = 0.51
Birth order			
Triplet A	194	1907 ± 538	
Triplet B	193	1850 ± 543	
Triplet C	193	1837 ± 548	
		p = 0.40	
Zygosity			
Spontaneous same-sex	51	5772 ± 1471	33.2 ± 3.5
Spontaneous mixed-sex, induced and IVF	137	5584 ± 1466	33.8 ± 2.9
		p = 0.036	p = 0.016

The one-way analysis of variance indicated that fetal gender, maternal parity, and the etiology of the triplet gestation all affect triplet birth weight. Because of the potential interrelationship of these variables, a three-way analysis of variance exploring the effect of fetal gender, parity, and etiology on triplet birth weight is presented in Table 4. The significant effect of being a male fetus ($p = 0.007$) and maternal parity ($p = 0.02$) on combined birth weight was confirmed. However, the association of triplet etiology ($p = 0.15$) and birth weight was not significant. The analysis indicates that the effects of triplet etiology were the same for both genders ($p = 0.053$) and both states of maternal parity ($p = 0.54$).

Since preeclampsia is frequently a disease of the younger, nulliparous woman, the possible interrelationship of preeclampsia with both maternal age and parity was evaluated by the three-way analysis of variance. While 20 of the 30 women with preeclampsia

Table 4 - Effect of fetal gender, maternal parity and etiology on total triplet birth weight

Fetal gender	Nulliparous	Parous
Induced triplets		
MMM	4539 ± 1196	6282 ± 1386
MMF	5600 ± 1403	5646 ± 1938
MFF	5290 ± 1048	5931 ± 1197
FFF	4886 ± 1819	4309 ± 1123
Spontaneous triplets		
MMM	3969 ± 3695	6228 ± 1029
MMF	6584 ± 981	7058 ± 1718
MFF	5479 ± 592	5224 ± 1422
FFF	5157 ± 1074	5866 ± 1850

were nulliparous, there was no statistical association between preeclampsia and either parity ($p = 0.65$) or maternal age ($p = 0.94$) on combined triplet birth weight. Nor was there any significant interaction between all three variables and combined triplet birth weight ($p = 0.51$).

DISCUSSION

The impact of various maternal and fetal variables on triplet birth weight has been addressed in multiple prior reviews. Unfortunately, the inferences from most of these previous reviews were limited by the small number of triplets in these studies. As a result of these limitations, the literature is contradictory as to the effect of several maternal and fetal variables on triplet birth weight at delivery. In addition, no previous review of triplet gestations has enjoyed the accuracy in gestational age dating present in the current series. Over half of the triplets' gestational ages were determined based on the day of conception. The remaining gestational ages were determined no later than the end of the second trimester with dating confirmed by ultrasonic examination.

Consideration of fetal variables such as gender, birth order and zygosity, and maternal variables such as age, parity and etiology, have all been reported to have conflicting effects on triplet birth weight. The birth weight advantage for male triplets reported here substantiates the findings of other investigators such as Asaka et al [1] in Japan, Itzkowic [5] in London, and Loucopoulos and Jewelewicz [7] in New York. However, in a review of 31 triplets, Holcberg et al [4] found that male infants have a nonsignificant reduction in birth weight compared to their female counterparts.

Birth order has also been reported to have conflicting effects on triplet birth weight. Itzkowic [5] found the first triplet to be heaviest among his 59 sets, and Asaka et al [1]

noted that the first and second triplets were each heavier than the third in their review of 124 sets. The failure of birth order to affect overall birth weight in the current study supports the work of Holcberg et al [4], Loucopoulos and Jewelewicz [7], and a review of 367 triplets from South Africa by Deale and Cronje [3]. The heaviest infant did present first with a greater frequency than would otherwise be expected by chance alone. Rather than birth order having any specific effect on triplet birth weight, the situation may be that subtle differences in triplet weight has an effect on fetal presentation.

The precise determination of zygosity is rarely available in most clinical reviews. Zygosity is usually discussed in terms of outcome differences between same-sex and mixed-sex triplet sets. The obvious disadvantage of this approach is that the majority of same-sex triplets are not monozygotic. In fact, the majority of triplets are the result of monozygotic splitting of dizygotic twins. Despite this, both Asaka et al [1] and McKeown and Record [8] demonstrated a lower mean birth weight in same-sex triplets, possibly representing a negative influence of monozygosity. For purposes of this analysis, spontaneous same-sex triplet gestations were compared with spontaneous mixed-sex triplets, induced triplets and IVF triplets. Triplet zygosity, approximated in this way, was not significantly associated with either gestational age or birth weight at delivery. In fact, the spontaneous same-sex triplets were actually slightly heavier than those gestations known to be diovular or triovular. The discrepancy between these extensive reviews is unexplained and needs futher evaluation especially considering the increased frequency of both medically induced and in vitro multifetal gestations.

Daw [2] and Kurtz et al [6] both suggested women more than 30 years old had triplets that weighed more and enjoyed better perinatal survival. The correlation of maternal age with birth weight and gestational age in this report revealed nonsignificant associations. Kurtz et al [6] noted that only one of six primigravid women were able to carry their infants to term and suggested the possible beneficial effects of parity. Ron-el et al [10] noted that nulliparous women had significantly shorter gestations and lighter birth weights among his 19 triplets and 6 quadruplets. Daw [2], however, reported on 14 triplets and found that parity had no effect on birth weight or perinatal mortality. The present study identified a major beneficial effect of parity on combined birth weight that was independent of gestational age.

Recent reports have considered the influence of triplet etiology because of the significant impact of ovulation induction and in vitro fertilization on the frequency of triplet birth. Ron-el et al [10] noted that spontaneous triplet and quadruplet pregnancies lasted two weeks longer than induced gestations. Syrop and Varner [11] had similar results in a smaller review. Holcberg et al [4] found that their 21 spontaneous triplets delivered significantly earlier and weighed less than 10 induced triplets. In this review, the one-way analysis of variance suggested a birth weight and gestational age advantage for spontaneous triplets. However, when fetal gender and parity were included in a three-way analysis of variance, this advantage disappeared. It seems likely that this occurred because of the excessive number of parous women in the spontaneous-triplets group compared to the group requiring medical induction of ovulation or in vitro fertilization to assist with fertility.

Obviously, there are a number of other medical or obstetrical complications besides preeclampsia that may influence birth weight (eg, prepregnancy maternal weight, maternal weight gain during pregnancy, smoking, diabetes, anemia, socioeconomic status,

adequacy of prenatal care, etc), and unfortunately, these confounding variables cannot be controlled for in the present study. However, this study does address most of the clinical variables previously reported to have a significant effect on birth weight. It is hoped that the size of the current series and accuracy of the gestational dating may help clarify some of the controversies that exist in the literature which are probably due to data errors encountered in previous studies of limited size.

There is little controversy, however, that the most powerful variable affecting triplet birth weight is the occurrence of premature labor. Premature birth complicated most of these triplet gestations and preterm labor was the major contributing factor [9]. While gestational age was significantly correlated with triplet birth weight, being male and maternal parity each have beneficial effects on birth weight that are independent of gestational age. Triplet gestations resulting from ovulation induction or in vitro fertilization do not seem to enjoy any significant advantage or disadvantage in terms of birth weight or gestational age at delivery. These factors should all be considered when counseling women with triplets or when evaluating outcome data from future series of triplet birth.

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