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MATERNAL AND NEONATAL OUTCOME OF TRIPLET VERSUS TWIN AND SINGLETON PREGNANCIES

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Purpose: To determine the maternal complications and the neonatal outcome of triplet gestation and to compare the data with those from twins and singletons matched for gestational age.

Methods: In this retrospective chart review, 35 triplet pregnancies were compared with twin and singleton pregnancies that delivered closest to the sets of triplets under review. Statistical analyses were performed with chi-squared tests and Student's t-test; p values less than 0.05 were considered significant.

Results: Maternal age was significantly higher in triplets and twins compared to singletons: 27.4 ±4, 27.4 ±4.5, and 24 ±5.1, respectively ($p<0.001$). 30 /35 (85.7%) of the triplets were delivered by cesarean section, whereas 25/35 (73.5%) of the twins and 13/35 (34.2%) of the singletons were delivered by cesarean ($p<0.001$). There was increased maternal morbidity in triplet pregnancies like uterine atony, anemia, and febrile morbidity, but they did not reach statistical significance. Although all deliveries were preterm, in the evaluation of neonatal outcomes by 1 and 5 minute Apgar scores, singletons' 1 and 5 minute Apgar scores were significantly higher than those of twins and triplets ($p<0.005$). However, there was no statistically significant difference between twins and triplets according to their Apgar scores ($p>0.05$).

Conclusion: Iatrogenic multiple births are increasing as the use of assisted conception techniques expands. Increased obstetric risk such as threatened preterm delivery and cesarean section rate could be observed. The risks of maternal morbidity and obstetric complications are increased in triplet pregnancies. Therefore, we concluded that this study could be useful in counseling patients with respect to the anticipated perinatal outcome of triplet pregnancies.

Key Words: Triplet pregnancy, twin pregnancy, neonatal outcome, maternal outcome.

ÜÇÜZ GEBELİKLERİN İKİZ VE TEK GEBELİKLERLE MATERNAL VE NEONATAL SONUÇLARININ KARŞILAŞTIRILMASI

Amaç: Üçüz gebeliklerde neonatal sonuçları ve maternal komplikasyonları saptamak ve bunları ikiz ve tekiz gebeliklerle karşılaştırmak.

Metod: Bu retrospektif çalışmada otuz beş üçüz gebelik kayıtta en yakın sıradaki, gestasyonel yaşları uyumlu ikiz ve tekiz gebeliklerle eşleştirildi. İstatistik incelemeler ki-kare testi ve student-t testleri ile yapıldı, 0.05 altındaki p değerleri istatistiksel olarak anlamlı kabul edildi.

Bulgular: Maternal yaş üçüz ve ikizlerde tekizlere oranla anlamlı olarak fazla idi, sırasıyla 27,4 ±4, 27,4 ±4,5, 24 ±5,1 ($p<0,001$). Üçüz gebeliklerin 30/35 'i (%85,7) sezeryan ile sonlanırken ikizlerin 25/35 'i (%73,5), tekizlerin 13/35 'i (%34,2) sezeryan idi ($p<0,001$). Üçüz gebeliklerde uterin atoni, anemi, febril morbidite gibi artmış maternal morbidite vardı ancak bunlar istatistiksel olarak anlamlı değildi. Tüm doğumlar preterm idi; ancak 1. ve 5. dakika Apgar skorları ile neonatal sonuçlar değerlendirildiğinde, tekiz gebeliklerde 1. ve 5. dakika Apgar skorları ikiz ve üçüzlerden anlamlı olarak anlamlı olarak fazla idi ($p<0,005$). Ancak ikiz ve üçüzlerin Apgar skorları arasında anlamlı bir fark yoktu ($p>0,05$).

Sonuç: Yardımcı üreme tekniklerinin kullanımının artmasıyla iatrojenik çoğul gebeliklerin sıklığında artış olmuştur. Bu durumda preterm doğum, artmış sezeryan oranları gibi obstetrik risklerde artış söz konusudur. Üçüz gebeliklerde de maternal morbidite ve obstetrik komplikasyonlar daha sık karşımıza çıkar. Bu yazı, üçüz gebeliklerle ilgili ailelerin bilgilendirilmesi ve klinik öngörüde bulunulması noktasında fikir verici bir değer taşımaktadır.

Anahtar Kelimeler: üçüz gebelik, ikiz gebelik, neonatal sonuçlar, maternal sonuçlar

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INTRODUCTION

The incidence of high-order gestations (more than two fetuses) has increased significantly since the introduction of ovulation induction therapy and in vitro fertilization and embryo transfer (IVF-ET). An increase in the number of fetuses is associated with an increase in the frequency of maternal complications and higher perinatal mortality and morbidity (1).

Triplet pregnancies have an increased neonatal morbidity and mortality, mainly attributed to preterm birth and smallness for gestational age. Studies have indicated that triplet pregnancies have a lower chance of reaching term than singleton pregnancies (87.8% vs 9.7% prematurity rate) (2). Twins also have an increased perinatal morbidity compared to singletons, yet it is better than that of triplets (3). Birth order of twins and triplets was implicated as a factor contributing to the increased morbidity and mortality of the second or third newborns, favoring the first borns (4).

Many previous publications have stressed the higher incidences of prematurity, low birth weight (lbw), intrauterine growth retardation (IUGR), cesarean section, congenital anomalies, placenta previa and pregnancy induced hypertension after IVF-ET (5). On the other hand, triplet pregnancies face other hemorrhagic complications such as placental abruption and post-partum uterine atony, which increase the need for blood transfusions and cesarean hysterectomy (6).

The objective of the present study was to determine the maternal complications and the neonatal outcome of triplet gestation and to compare the data with those of twins and singletons matched for gestational age.

MATERIALS AND METHODS

A retrospective chart review of all triplets delivered by cesarean section or vaginally at Zekai Tahir Burak Women's Health Education and Research Hospital between 1 January 2000 and 1 January 2004 was performed and in this period 35 triplet deliveries were found. Before the study started, hospital ethics committee approval was obtained. No triplets delivered before 24 weeks survived; therefore, these pregnancies were excluded from our analysis. For comparison, a control group was established. This group comprised live born twins and singletons matched for gestational age and delivered closest to the sets of triplets under review. The gestational age at birth was calculated by adding 14 days to the day of ovum pick-up for the IVF-ET group; for the spontaneous conception group, the first day of the last menstrual period was used and, if possible, first trimester ultrasonographic findings. We did not match maternal characteristics to the controls with respect to maternal age, race, IVF/non-IVF pregnancy and mode of delivery.

Presentations and order of delivery were documented by the surgeon. Neonatal complications were recorded from the newborns' charts. Prematurity was defined as delivery before 37 weeks of gestation. Preterm rupture of membranes (PROM) was defined as rupture of membranes prior to 37 weeks' gestation. Postpartum febrile morbidity was defined as persistent maternal fever more than 38 ºC for more than 24 h post-partum requiring investigation and treatment. Very low birth weight (vlbw) was defined as birth weight less than 1500 g, while lbw was defined as birth weight less than 2500 g. Corticosteroid therapy was administered to women at less than 34 weeks where delivery was thought imminent. Intrauterine growth restriction was defined as weight <10th percentile. Necrotizing enterocolitis was diagnosed clinically by the neonatologist and pediatric surgical staff. Survival was defined as the percentage of infants alive at hospital discharge. Hypertension was diagnosed with persistent blood pressure of ≥ 140/90 mmHg and anemia when hemoglobin was ≤10 g/dl. Morbidity and mortality were compared between triplet, twin and singleton infants. Statistical analyses were performed with chi-squared tests and Student's t-test; p values less than 0.05 were considered significant.

RESULTS

Gestational age at delivery, the newborns' weight and maternal age are presented in Table 1. The mean birth weights of singletons and twins were higher than those of triplets and the difference was statistically significant (p<0.001). Maternal age was significantly higher in triplets and twins compared to singletons (p<0.001).

As seen, 85.7% of the triplets were delivered by cesarean section, whereas 73.5% of the twins and 34.2% of the singletons were delivered by this method (p<0.001). In addition, 94.3% of the triplet pregnancies were the result of IVF, while only 11.4% twins were the result of this technique. There were no IVF pregnancies in the singleton group (p<0.001).

Neonatal outcomes according to 1 and 5 minute Apgar scores are shown in Table 2. Singletons' 1 and 5 minute Apgar scores were significantly higher than those of twins and triplets (p<0.005). However, there was no statistically significant difference between twins and triplets according to their Apgar scores (p>0.05). Only one fetal anomaly was observed and it was in the singleton group; this baby was born with ambiguous genitalia. Because all of the twin and singleton pregnancies were matched with triplets for gestational age all deliveries were preterm.

Table 2. Newborns' Apgar scores in the three groups.

Triplet (n=35)	Twin (n=35)	Singleton (n=35)
APGAR 1 minute	5.2 ± 1.8	5.7 ± 1.5 6.5 ± 0.8
APGAR 5 minute	7.1 ± 2.1	7.7 ± 1.4 8.5 ± 0.9

The percentage of triplets receiving prenatal steroid was similar to that of twins and singletons. In triplet pregnancies admission to the neonatal intensive care unit (NICU) was significantly higher than in twin and singleton pregnancies (p<0.001) and admission rates to the NICU for singleton, twin and triplet newborns were 39.5%, 85.3% and 100%, respectively. In triplet and twin pregnancies the most frequent NICU admission indications were vlbw and respiratory distress (rd), and for the singleton group it was lbw; no newborns were admitted to the NICU with vlbw and rd indications. Necrotizing enterocolitis (NEC) was diagnosed in 2 (1.9%) triplet infants, and one of the twins developed NEC. Four (3.8%) of the triplet infants had retinopathy of prematurity (rp), while one of the twins and one of the singletons had it (p>0.05). Mean duration of hospitalization for triplet infants was 16.3±18.5 days, for twins 14.8±15.3 days, and for singletons 13.9±14.1 days (p>0.05). In triplet pregnancies 85.7% of deliveries were by cesarean section and mean gestational age of the cesarean group was 32.03 ± 2.29 weeks and mean gestational age of the vaginally delivered group was 26 ± 1.9 weeks. When we eva-

Table 1. Pregnancy characteristics and birth weights in the three groups.

	Triplets (n=35)	Twins (n=35)	Singletons (n=35)	p values
Gestational age (weeks) (mean ± SD)	31.1 ± 3.2 (26 – 35 w)	32 ± 2.5 (27 – 35 w)	31.3 ± 1.8 (28 – 34 w)	>0.05
Birth weight (gram) (mean ± SD)	1403 ± 517 (590 – 2400 g)	1807 ± 499 (750 – 2920 g)	2343 ± 301 (1650 – 2900 g)	<0.001
Maternal age (year)	27.4 ± 4.4	27.4 ± 4.5	24 ± 5.1	<0.001
Cesarean section (n)	30 /35 (85.7%)	25 /35 (71.4%)	13/35 (37.1%)	<0.001
IVF pregnancy	33 /35 (94.3%)	4 /35 (11.4%)	0 /35 (0%)	<0.001
Prenatal steroid (n)	31/35 (88.5%)	29/35 (82.8%)	35/35 (100%)	>0.05

Table 3. Maternal complications.

	Triplets (n=35)	Twins (n=35)	Singletons (n=35)	p values
Atony (n)	4 (11.4%)	1 (2.8 %)	1 (2.8%)	>0.05
PROM	7/35 (20%)	5/35 (14.2%)	3/35 (8.5%)	>0.05
Anemia (Hb <10 g)	9/35 (25.7%)	6/35 (17.1%)	4/35 (11.4%)	>0.05
Febrile morbidity	4/35 (11.4)	2/35 (5.7%)	2/35 (5.7%)	>0.05

luate the Apgar scores of the two groups in triplet pregnancies, 1 minute Apgar score was 2.9±1.7 and 5 minute Apgar score was 4.3±2.7 in the vaginally delivered group; these scores were 5.6±1.5 and 7.5±1.6, respectively, in the cesarean group. This shows a statistically significant difference between the two groups in terms of Apgar scores ($p<0.001$).

Maternal complications are shown in Table 3. Anemia was the most common maternal complication in all groups. Uterine atony was seen in 4 patients (11.4%) in the triplet group, 1 patient (2.8%) in the twin group and 1 patient (2.8%) in the singleton group ($p>0.05$). One patient needed a blood transfusion because of postpartum hemorrhage in the triplet group. Additionally acute hepatitis was seen in one patient in the triplet group ($p>0.05$). There was no maternal mortality in the three groups.

DISCUSSION

The purpose of this study was to assess the maternal and perinatal mortality and morbidity using a matched comparison of triplet to twin and singleton pregnancies. Multifetal gestations, especially triplet and higher order gestations, have been associated with a high incidence of perinatal and neonatal morbidity and mortality especially because of premature delivery (7).

When the number of fetuses increases, the duration of gestation and birth weight decrease. The method of delivery of triplet pregnancies remains controversial, although most authors advocate cesarean section (8), believing that this reduces the frequency of in utero fetal death and obstetrical accidents and enables optimization of neonatal conditions for programmed birth. In many studies, in triplets >26 weeks' gestation delivering by cesarean section was thought to be better. Weissman et al., in a comparison of 39 triplets with matched control twins, reported that mortality was twice as high in triplets that were delivered vaginally (3). Furthermore, in the current study, Apgar scores of triplet babies delivered by cesarean section were significantly higher than those of the babies delivered vaginally. This may show the superiority of cesarean section to vaginal delivery for triplet pregnancies but a more probable explanation for this may be the advanced gestational weeks of the patients in which delivery was by cesarean section.

Several studies have reported cesarean section rates differing from 1.6% to 78%, compared with 85.7% in this study (7). Since our establishment is a tertiary center, we encounter complicated pregnancies often requiring intervention and hence cesarean section. In our study group, five women delivered vaginally, and all had less than 28 weeks' gestations. The decisions to proceed with vaginal deliveries in these women were made in the belief that the probability of neonatal survival was low and that vaginal delivery caused lower short- and long-term maternal complications.

Concerning neonatal mortality, like Zanconato et al. we did not observe any deaths during the hospitalization period among the triplets >26 weeks gestation, unlike the corresponding figure of 3.8% derived from another series (6).

Most previously published studies did not include a control group subjected to similar management practices for comparison with triplets (9). With the current study we were able to provide similar obstetric and neonatal management to singleton, twin and triplet pregnancies in a single hospital in a short time and we had the chance to record gestational age and compare the outcome data of triplets with those of twins and singletons.

Maayan-Metzger et al. and Ballabh et al. found no difference in outcome for triplets based on birth order, as in our study group (2,10). The similar outcomes based on birth order seen in this population are most probably due to the fact that we deliver all viable triplets by cesarean section.

Women who become pregnant after ART are usually older than average; the proportion of elderly primigravid patients over the age of 35 years is fairly high. It is generally accepted that older women are more prone to obstetric problems, although some studies confirm this only in part (5). The major factor contributing to an adverse pregnancy or obstetric outcome of ART as compared with a population-based control is the increased incidence of multiple pregnancy. Our study found that women with triplet pregnancies were associated with increased risks of maternal morbidity including anemia, uterine atony, and increased cesarean delivery, but these complications were not statistically significant except for increased cesarean delivery. Induction and vacuum/forceps were used less commonly in women with triplet pregnancies.

In this cohort, nearly all (94.3%) of the triplet pregnancies resulted from assisted reproductive techniques and there were no IVF pregnancies in the singleton group. Because of the increased risks associated with higher order multiple pregnancy, it is now widely accepted that the transfer of more than two embryos is problematic (11), and so it is likely that the incidence of triplets will decline over the coming years. Moreover, fetal reduction procedures may be a rational choice

in triplet and high order pregnancies. Proper counseling about these subjects should be offered to patients.

It appears that outcome is primarily dependent on gestational age. It seems that the major factors responsible for the improved fetal and maternal outcome include early diagnosis, meticulous antenatal care, early hospitalization, frequent evaluation of fetal well being, delivery by cesarean section and a functional intensive care unit.

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