OBSTETRICS

Perinatal and obstetric outcomes of dichorionic vs trichorionic triplet pregnancies

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BACKGROUND: Clinical management and outcome of multiple gestation can be affected by chorionicity. In triplet pregnancies, fetal death has been associated with dichorionic (DC) and monochorionic placentation. Studies evaluating triplet pregnancy outcomes in relation to chorionicity have been few and may not reflect contemporary antenatal and neonatal care.

OBJECTIVE: The objective of this study was to compare obstetric and perinatal outcomes in DC and trichorionic (TC) triplet pregnancies.

STUDY DESIGN: We performed a retrospective cohort study of triplet pregnancies that delivered at ≥20 weeks' gestation at 2 Chicago area hospitals from January 1999 through December 2010. Chorionicity was determined by pathology specimen. Maternal and infant charts were reviewed for obstetric and perinatal outcomes.

RESULTS: The study population included 159 pregnancies (477 neonates) of which 108 were TC (67.9%) and 51 were DC (32.1%). Over 94% of mothers in this study had all 3 infants survive to discharge regardless of chorionicity. No difference was found in perinatal mortality rate between DC and TC triplets (3.3% vs 4.6%; $P = .3$). DC triplets were significantly more likely to be very low birthweight (41.8% vs 22.2%; odds ratio, 2.2; 95% confidence interval, 1.2—4.2; $P = .02$) and to deliver at <30 weeks (25.5% vs 8.3%; odds ratio, 6.1; 95% confidence interval, 1.9—19.4; $P = .002$) compared to TC triplets. Criteria for twin-twin transfusion syndrome (TTTS) were present in 3 DC triplet pregnancies (5.9%). Neonates in pregnancies complicated by TTTS were less likely to survive 28 days as compared to neonates from DC pregnancies that were not affected by TTTS ($P = .02$) or TC neonates ($P = .02$) Neonatal survival was similar in DC pregnancies not affected by TTTS and TC pregnancies (98.6% and 96.6%; $P = .7$).

CONCLUSION: Although perinatal mortality did not correlate with chorionicity, DC pregnancies were more likely to deliver <30 weeks' gestational age and have very low birthweight neonates. Neonatal mortality appears to be mediated by the presence or absence of TTTS as 28-day survival was worse in DC pregnancies complicated by TTTS, but similar between DC pregnancies not affected by TTTS and TC pregnancies.

Key words: chorionicity, perinatal and obstetric outcome, triplets

Introduction

Clinical management and outcome of multiple gestation can be affected by chorionicity.[1] Monochorionicity has been linked to higher neonatal morbidity and mortality rates associated with prematurity, low birthweight (LBW), and intrauterine death in twin gestations.[2] In triplet pregnancies, fetal death has been associated with dichorionic (DC) and monochorionic (MC) placentation. Perinatal deaths related to MC or DC placentation are often attributed to anomalous intertwin placental vascular anastomoses, which can progress to twin-twin transfusion syndrome (TTTS).[1-5] Furthermore, selective intrauterine growth restriction (IUGR) from discordant placental sharing can increase perinatal mortality in MC and DC pregnancies.[6] A recent comparison of DC and trichorionic (TC) triplets noted an 8 times higher perinatal mortality rate in DC triplets.[7] Unfortunately, no specific changes in antenatal care and monitoring have been associated with significant improvement in MC and DC triplet pregnancy outcomes; even with frequent antenatal monitoring, intrauterine fetal death (IUFD) or perinatal death cannot be reliably predicted.[5,6,8-10]

Studies evaluating triplet pregnancy outcomes in relation to chorionicity have been few and may not reflect contemporary antenatal and neonatal care.[7,11-13] One of 2 studies spanning the last decade found significant differences in weight and gestational age (GA) at delivery in DC triplets compared to TC triplets; however, no substantial evaluation of neonatal morbidities was performed.[14] The other study evaluated triplet pregnancies by chorionicity with the primary outcome of perinatal death. Although they found a significant difference in the risk of death in MC triplets compared to TC triplets, there was no significant difference found between DC and TC triplets. Furthermore, evaluation of obstetric and neonatal outcomes were not described.[5] Therefore, the objective of this study was to further examine the perinatal and obstetric outcomes in a contemporary cohort of DC and TC triplets.

Materials and Methods

We performed a retrospective cohort study of deliveries at NorthShore University HealthSystem and the University of Chicago Hospital. The study population included all triplet pregnancies with a placental pathology specimen delivered at ≥20 weeks' gestation receiving perinatal care at our facilities from Jan. 1, 1999, through Dec. 31, 2010. Pregnancies that delivered at <20 weeks' gestation, were MC, underwent fetal reduction, or had known fetal anomalies were excluded. We excluded MC pregnancies as there were only 4 such pregnancies in the cohort limiting the ability to make meaningful comparisons to the DC and TC groups. Additionally, we

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opted against combining MC and DC pregnancies as MC triplets have been reported to have a substantially increased mortality rate.[5] Estimated GA was calculated according to American Congress of Obstetricians and Gynecologists criteria at both institutions.[15] Chorionicity was determined by early ultrasound and confirmed by pathology specimen. The study was approved by the institutional review board at both hospitals (NorthShore University HealthSystem 11-185, University of Chicago 13-1132).

Maternal data were abstracted from hospital charts and each hospital's pathology database. Baseline data collected included: demographic data (age, race/ethnicity, parity, history of preterm birth, and maternal comorbidities), placentation, and use of assisted reproductive technology (ART). Specific types of ART were not identifiable and were thus categorized collectively as ART. Outcome data included mode of delivery, GA at delivery, and birthweight at delivery. The exact indication for delivery could not be identified in all pregnancies. Antepartum complications were abstracted from admission and discharge diagnoses and included TTTS, IUFD, antenatal bleeding requiring admission, preterm premature rupture of membranes (PPROM), preterm labor (PTL), and preeclampsia. We assessed intertriplet discordance in both DC and TC pregnancies as a surrogate marker of selective IUGR. Intertriplet discordance was present if there was a 25% discordance between the largest and smallest triplet as calculated by the birthweight of the largest triplet minus smallest triplet divided by largest triplet. The diagnosis of TTTS was made by standard ultrasound criteria of polyhydramnios (deepest vertical pocket >8 cm) and oligohydramnios (deepest vertical pocket <2 cm) in the MC pair as defined by Quintero et al[16] and confirmed by pathology.

Neonatal outcome data were abstracted from both the mother and infant chart to ensure concordance. Neonatal data collected included birthweight, Apgar scores, neonatal intensive care unit (NICU) admission, number of days spent in the NICU, respiratory distress syndrome, intraventricular hemorrhage, necrotizing enterocolitis, retinopathy of prematurity, patent ductus arteriosus, sepsis, anemia, hypoglycemia, and neonatal demise (NND) (death within 28 days of birth).

Continuous variables were reported as mean ± SD and median (range). The normality assumption for continuous variables was assessed using the Shapiro-Wilk test. Continuous variables were compared between DC and TC groups by 2-sample *t* test or Wilcoxon rank sum test as appropriate. Categorical variables were reported as frequency (percentage) and were analyzed by χ^2 tests or Fisher exact test for 2-group comparisons. A multivariable logistic regression model was built to compare maternal outcomes and babies' outcomes between DC and TC groups with adjustment for confounding factors. The covariates adjusted for the DC and TC comparison were selected based on statistical and clinical relevance. Any clinically relevant covariates were potential confounders. Statistically, a covariate is defined as a confounder and will be retained in the final model if it changes regression coefficients of logistic regression by 10%. Any covariate satisfying this criterion was adjusted for the group comparison. Akaike information criterion and likelihood ratios test were also adopted for model evaluation and covariate selections. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were reported with *P* values.

To analyze the risk associated with TTTS, the DC group was separated into pregnancies with TTTS and pregnancies without TTTS. Multivariable Cox proportional hazard regression model were used to compare time-to-event incidence rates: (1) between DC-TC groups; and (2) among DC-TTTS, DC-non-TTTS, and TC groups for NND with adjustment of potential confounders. We visualized the 28-day neonatal survival distribution using Kaplan-Meier curves, and the log rank test was used to compare the overall survival distribution across groups. *P* values were adjusted for multiple comparisons. Statistical analyses were performed on software (SAS 9.3 Windows platform; SAS Institute, Cary, NC). $P < .05$ was considered as statistically significant.

Results

From Jan. 1, 1999, through Dec. 31, 2010, 191 triplet pregnancies were documented via pathology report. Patients were excluded if they delivered <20 weeks (n = 8), had reduction from triplets to twins or singleton (n = 14; 2 DC and 12 TC, all elective and performed in the first trimester), had known fetal anomalies (n = 6), or were MC (n = 4). There were no cases of TTTS in our cohort <20 weeks. There were 159 pregnancies (477 neonates) of which 108 were TC (67.9%) and 51 were DC (32.1%). In general, women were 32.5 ± 5 years old, nulliparous (n = 91, 57.2%), and used ART (n = 130, 81.8%). Common antenatal complications were PTL (n = 79, 49.7%), preeclampsia (n = 49, 30.8%), and PPROM (n = 38, 23.9%). Most deliveries were preterm, with almost half delivering <34 weeks (n = 77, 48.4%). Indication for delivery was often secondary to progression of labor in patients who presented in PTL or with PPROM. Only 7 pregnancies underwent delivery secondary to nonreassuring fetal well-being of which 6 were TC and 1 was DC. Although there were 3 IUFDs and 17 NND, most women (94%) had all 3 babies survive to discharge. Of the live-born infants, 441 (92.5%) were LBW (<2500 g), 136 (28.5%) were very LBW (VLBW) (<1500 g), and 47 (9.9%) were extremely LBW (<1000 g). Prematurity was the number-one reason for admission to NICU, affecting 72.5% of all neonates.

A comparison between baseline maternal characteristics in DC and TC pregnancies is shown in Table 1. Women with DC pregnancies were slightly younger (31.2 ± 5.9 vs 33.1 ± 4.4 years, $P = .05$), less likely to use ART ($P = .04$), and more likely to require betamethasone (74.5% vs 53.7%; OR, 3.2; 95% CI, 1.4−6.9; $P = .004$) than women with TC pregnancies. They did not significantly differ in other baseline characteristics including race, parity, and maternal comorbidities. Antepartum