Impact of induced pregnancies in the obstetrical outcome of twin pregnancies

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Objective: To compare obstetric outcomes of induced twins with those spontaneously conceived.
Design: A prospective observational study was conducted in twin pregnancies delivered over 16 years.
Setting: A tertiary obstetric center with differentiated perinatal support.
Patient(s): A total of 180 induced twins and 698 spontaneously conceived were included.
Intervention(s): None.
Main Outcome Measure(s): Comparison of demographic factors, obstetrical complications, gestational age at delivery, mode of delivery, birth weight, and immediate newborn outcome.
Result(s): First-trimester bleeding was higher in the induced group (6.0% vs. 12.2%), as were gestational diabetes (4.4% vs. 8.3%) and discordant intrauterine growth (4.3% vs. 11.1%). Preterm premature rupture of membranes was less frequent (23.9% vs. 12.8%) as was preterm delivery $\leq$32 weeks (22.5% vs. 14.0%). Cesarean section rate was higher (50.6% vs. 63.9%). Other obstetrical complications, newborn data, and puerperal complications were not statistically different. Except for first-trimester bleeding (significantly associated with monochorionicity), these results were independent from chorionicity. Regarding the induced method (ovulation induction, IVF, or ICSI), IVF is a predictor for first-trimester bleeding and IVF or ICSI a predictor for cesarean section.
Conclusion(s): The higher rates found with induced twins of first-trimester bleeding, gestational diabetes, and discordant growth do not contribute to different neonatal immediate outcomes and do not contribute to higher rates of prematurity, low birth weight, or other major perinatal complications. (Fertil Steril® 2014;101:172–7. ©2014 by American Society for Reproductive Medicine.)
Key Words: Twins, induced reproduction, obstetrical outcomes

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Since 1980 there has been a worldwide increase in multiple births. This seems to be due to an increase in the age of women at reproduction, the use of ovulation induction (OI), and the use of assisted reproduction techniques (ART), such as in vitro fertilization (IVF) and intracytoplasmatic sperm injection (ICSI). ART has become a widespread option for the treatment of human infertility, and data show that ~22% of all deliveries after ART occur in pregnancies with more than one fetus: 20.7% of twins and 1% of triplets (1).

It is well known that maternal and obstetrical complications are more frequent in twin pregnancies than in singleton pregnancies. However, it is not yet clear if induced twin pregnancies must be considered to be at higher obstetrical risk than spontaneously conceived ones. Studies comparing the outcome of induced twin pregnancies and those of spontaneous conception report inconsistent findings; some report similar perinatal outcomes (2–5), whereas others report a higher risk of adverse perinatal outcomes, such as gestational diabetes, hypertension, intrauterine growth discordance, preterm birth and cesarean section, low birth weight, and higher neonatal intensive care unit (NICU) admissions (6–14), and others find a better perinatal outcome after IVF/ICSI (15).

In most studies, however, only IVF/ICSI are evaluated, leaving out OI, and chorionicity, considered to be a confounding factor in predicting the perinatal outcomes of twin pregnancies, has not been determined or evaluated.

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The aim of the present study was to compare obstetrical outcomes of induced twin pregnancies with those spontaneously conceived, and to evaluate the impact of chorionicity and the type of induction (OI, IVF, or ICSI) on the results.

MATERIALS AND METHODS

Data from files of all twin pregnancies that were delivered in our tertiary obstetrics center with differentiated perinatal support over a period of 16 years (from January 1996 to December 2011) were prospectively collected and analyzed. No intervention was done besides the normal twin surveillance protocol in those with surveillance in our center. This study was included in an investigation project approved by the Ethics Committee of the University Hospitals of Coimbra.

We excluded triplets, higher orders, and monoamniotic multiple gestations from the analysis. All twin pregnancies (dichorionic and monochorionic) that were spontaneously conceived and those obtained following an induction method/technique—OI, IVF, or ICSI—were included.

In a first analysis, two groups were formed: one of all spontaneously conceived twin pregnancies and the other of all induced twin pregnancies. In both groups the following parameters were analyzed and compared: maternal age (categorized in the following classes <18, 18–25, 26–35, 36–40, and >40 years), parity, personal or family history of twins, personal disease history, and habits (current or earlier use of smoking, drugs, or alcohol).

Obstetrical complications included were first-trimester bleeding; urinary, genital, or other infections; anemia; fetal malformations; hypertensive diseases of the pregnancy (gestational hypertension, preeclampsia, eclampsia, and HELLP [hemolysis, elevated liver enzymes, and low platelet count] syndrome); gestational diabetes [GD]; preterm delivery [PTD], defined as delivery after 24 and before 37 weeks of gestation; preterm premature rupture of membranes (PPROM), defined as the occurrence of premature rupture of membranes after 24 and before 37 weeks of gestation; intrauterine growth restriction [IUGR], defined as fetal measure of abdominal perimeter <10th percentile; discordant growth, defined as 20% difference between fetal birthweights; and fetal death.

Birth data analyzed included gestational age at delivery (categorized in the following classes: <28, 28–32, 33–34, 35–36, and >36 weeks), mode of delivery (categorized as vaginal, cesarean section during delivery, elective cesarean section, and cesarian section of the second twin), birthweights of both twins, Apgar (American Pediatric Gross Assessment Record) score at 1st and 5th minute of both twins, and admission of the neonates in the NICU.

Puerperal complication occurrences were also analyzed: anemia, hemorrhage, hypertension complications, and endometritis.

Gestational age was calculated from the date of embryo transfer for the induced pregnancies obtained from ART and from the date of the last menstrual period in the spontaneously conceived group, both confirmed and corrected by the time of the first-trimester ultrasound. Chorionicity was also determined in the first-trimester scan (by lambda and T signs). In a second phase we went on to analyze the influence of chorionicity and of the type of induced technique (IO, IVF, or ICSI) in the above conditions.

A global characterization of the sample (180 induced and 698 spontaneously conceived twin pregnancies) was performed considering the above listed parameters. Categoric variables were characterized by absolute frequencies and relative frequencies, and continuous variables were characterized with the use of mean, standard deviation, quartiles, minimum, and maximum.

For categoric variables, differences in proportions between the two groups were evaluated with the use of the chi-square test or Fisher exact test. For continuous variables, the *t* test was used to compare means between the two groups and, when the assumptions for use of the *t* test were not satisfied, the Mann-Whitney test to compare the distribution of values. The normal distribution of values for continuous variables and the equality of their variances were tested with the use of the Kolmogorov-Smirnov and Levene tests, respectively. To analyze the stratification of risks according to age and chorionicity, the Breslow-Day test was used. A logistic regression model adjusted for age and chorionicity was made to look for predictors of the significantly different results found previously. The variables assumed as potential predictors were the type of pregnancy, induced method/technique, and all other variables included in the personal history and obstetrical complications. The significance level used in this analysis was 5%. The statistical software SPSS v19.0.0.2 was used.

RESULTS

During the period in study—January 1996 to December 2011—there were 878 deliveries of twin pregnancies in our center. Regarding the type of conception, 698 were spontaneous (79.5%) and 180 were induced (20.5%).

Over the period studied we found a significant growing trend for induced twin pregnancies ($P=.001$), which represented 20.3% of twin deliveries in our center. This trend is no longer observed regarding the mode of conception individually over the years, which remained stable: OI accounting for 31.5% of the induced pregnancies, IVF 41%, and ICSI 27.5%.

Maternal characteristics in both groups were analyzed (Table 1). As expected, women in the induced group were significantly older, had higher rates of infertility, and most were nulliparous.

There were no significant differences regarding personal medical histories (hypertensive, endocrine, renal, or other systemic disease) or habits (tobacco, alcohol, drugs).

The analysis of obstetrical complications (Table 2; anemia, infections, hypertensive disorders of pregnancy, fetal malformations, intrauterine fetal death, and IUGR) revealed no major statistically significant differences between the two groups.

First-trimester bleeding was higher in the induced group [6.0% vs. 12.2%; $P=.004$; odds ratio [OR] 2.18 (95% confidence interval [CI] 1.26–3.75)], as were gestational diabetes [4.4% vs. 8.3%; $P=.037$; OR 1.96 (1.03–3.71)] and intrauterine discordant growth [4.3% vs. 11.1%, $P<.001$; OR 2.78 (1.54–5.03)].