Obstetric and neonatal outcome after assisted fertilization and spontaneous conception: a comparative study

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Summary

Purpose: The widespread use of assisted reproduction technology (ART) is accompanied by concerns for potential adverse outcomes. The aim of the present study was to evaluate the impact of ART in obstetric and neonatal outcome. *Methods:* Data from labor ward records from 913 consecutive births were analyzed retrospectively, and the obstetric and neonatal outcomes of pregnancies after ART were compared with those after natural conception. *Results:* No major complications were noted after ART. A higher probability of cesarean section, lower gestational age at birth, lower birth weight and hospitalization in the Neontal Intensive Care Unit (NICU) was noted after ART, as compared with spontaneous conception. However, after exclusion of multifetal pregnancies, there was no significant difference in outcomes, except for cesarean section rates. *Conclusions:* The higher proportion of multiple pregnancies after ART is associated with lower gestational age at birth, lower birth weights and higher NICU hospitalization rates.

Key words: Obstetric outcome; Neonatal outcome; Assisted reproductive technology (ART); Assisted fertilization; Spontaneous conception.

Introduction

The use of assisted reproductive technology (ART) has been steadily increasing in Western countries during the last decades [1, 2]. The main reason for this trend appears to be the ever increasing number of women in developed countries who delay pregnancy until an age when fertility is physiologically reduced. This phenomenon is further enforced by the advances and availability of ART itself [3]. A major concern arising from the widespread use of ART is the potential risk of poor obstetric and postnatal outcomes after assisted fertilization, as compared with spontaneous conception. However, it is not clear if the causes of such adverse outcomes lie in ART or infertility itself and/or the etiology of infertility [3-5]. Furthermore, though it is well established that iatrogenic multifetal pregnancies lead to increased morbidity after assisted fertilization, it is not yet clear to what extent singleton pregnancies might lead to increased morbidity as well [3, 4]. In the present study, the obstetric and neonatal outcomes of births from pregnancies after use of ART were compared to those of pregnancies after natural conception.

Materials and Methods

Study population

Data from 913 consecutive pregnancies were analyzed retrospectively. Data was retrieved from labor ward records, containing information about pregnancies beyond 24 weeks gestation ending in birth (either live or stillbirth). Obstetric and neonatal outcomes in pregnancies after use of ART were compared with those after spontaneous conception in both multiple and singleton (n = 913), as well as in singleton pregnancies only (n = 863), after exclusion of multiple pregnancies. Obstetric outcome was compared in terms of mode of delivery and gestational age at birth; neonatal outcome was compared in terms of birth weight and days of hospitalization in the Neonatal Intensive Care Unit (NICU). Infertility treatment and obstetric management were conducted in all cases by one consultant in a single IVF-center and a single medical center for obstetric care. Prenatal screening for fetal anomalies was also performed by one specialist.

Statistical analysis

Linear or logistic regression analyses were conducted to adjust for covariates when the outcome was continuous or binary, respectively. The independent samples t-test was used to check for differences of continuous variables (e.g., mean days in NICU). The chi-square test was used to check for independence of nominal variables. P values less than 0.05 were considered statistically significant. SPSS version 16.0 (Chicago, IL, USA) was used for the analyses.

Results

Patient characteristics

An overview of descriptive statistical data from all singleton and multiple pregnancies ending in birth regarding maternal age, parity, mode of delivery, gestational age at birth, birth weight, and hospitalization in the NICU after assisted fertilization or spontaneous conception is presented in Table 1. After exclusion of multiple pregnancies, an overview of similar data from singleton pregnancies is presented in Table 2. No data from first and second trimester miscarriages were available in labor ward records.

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Table 1. — *Overview of data from all pregnancies (multiple and singleton).*

	Assisted fertilization	Spontaneous conception
Number of pregnancies	126	787
Number of neonates	160	804
Mean maternal age	35.6 (± 4.9)	32.5 (± 4.2)
Parity		
Para 0	104	413
Para ≥ 1	22	374
Mode of delivery		
Vaginal	27	413
Cesarean	99	374
Gestational age at birth	36.5 (± 1.8)	37.2 (± 1.6)
≥ 37 weeks	83	663
< 37 weeks	43	124
Birth weight		
Mean	2,645.2 (± 661.7)	3,039.2 (± 503.7)
≥ 2,500 g	103	719
< 2,500 g	57	85
NICU*	46	88

* Number of neonates hospitalized.

Table 2. — *Overview of data from singleton pregnancies only.*

	Assisted fertilization	Spontaneous conception
Number of pregnancies	93	770
Mean maternal age	35.7 (± 4.9)	32.4 (± 4.2)
Parity		
Para 0	80	402
Para ≥ 1	13	368
Mode of delivery		
Vaginal	27	413
Cesarean	66	357
Gestational age at birth	37.1 (± 1.4)	37.3 (± 1.3)
≥ 37 weeks	72	649
< 37 weeks	21	121
Birth weight		
Mean	2,999.9 (± 483.9)	3,079.7 (± 461.7)
≥ 2,500 g	82	707
< 2,500 g	11	63
NICU*	12	78

* Number of neonates hospitalized.

Data from 913 consecutive births were analyzed; 126 after assisted fertilization (13.8%) with 160 neonates and 787 after spontaneous conception (86.2%) with 804 neonates. Overall, there were 863 singleton (94.5%) and 50 multiple pregnancies (5.5%); there were 93 singleton (73.8%) and 33 multiple pregnancies (26.2%; 31 twins and two triplets) after use of ART and 770 singleton (97.8%) and 17 multiple pregnancies (2.2%; all twins) after natural conception. The mean maternal age was 33.0 years overall; 35.6 after assisted fertilization and 32.5 years after spontaneous conception.

Mode of delivery

Cesarean section was performed in all multiple pregnancies, regardless of the mode of conception. In singleton pregnancies, cesarean section was performed in most cases after use of ART (in 66 out of 93 cases – 71%). In contrast, vaginal delivery was the mode of delivery in most cases of singleton pregnancies after spontaneous conception (in 413 out of 770 cases – 53.6%). Using logistic regression analysis adjusted for maternal age and parity, we found that delivery by cesarean section was more likely than vaginal delivery (including operative vaginal delivery) in pregnancies after assisted fertilization as compared with pregnancies after spontaneous conception (OR 3.64, 95% CI; $p < 0.0001$). Exclusion of multiple pregnancies from this analysis did not alter conclusions (OR 1.87, 95% CI; $p < 0.014$).

Gestational age

For both singleton and multiple pregnancies mean gestational age at birth was 36.5 (± 1.8) after use of ART and 37.2 (± 1.6) after spontaneous conception; after exclusion of multiple pregnancies, mean gestational age at birth for singletons was 37.1 (± 1.4) and 37.3 (± 1.3), respectively. Preterm birth rates (i.e. birth before 37 weeks of gestation) after assisted fertilization or spontaneous conception were as follows: 1) for singletons 21 out of 93 (22.6%) and 121 out of 770 (15.7%), respectively, and 2) for multiple pregnancies 22 out of 33 (66.7%) and three out of 17 (17.6%), respectively.

Using linear regression analysis adjusted for maternal age and parity, we found that gestational age at birth was significantly higher in spontaneously conceived pregnancies than in pregnancies after use of ART (0.9 weeks, R = 0.239). Using an independent samples t-test this association remained statistically significant ($p < 0.005$). In singleton pregnancies however, linear regression analysis adjusted for maternal age and parity showed that gestational age at birth was not significantly related with the mode of conception. Furthermore, using Pearson's χ^2-test, there was no significant difference in the occurrence of preterm births (i.e. birth prior to 37 weeks of gestation) between the two groups.

Birth weight

For both singleton and multiple pregnancies mean birth weight was 2,645.2 g (± 661.7) after assisted fertilization and 3,039.2 g (± 503.7) after spontaneous conception; after exclusion of multiple pregnancies, mean birth weight was 2,999.9 g (± 483.9) and 3,079.7 g (± 461.7), respectively. Low birth weight rates (i.e. below 2,500 g) after use of ART or spontaneous conception were as follows: 1) for singletons 11 out of 93 (11.8%) and 63 out of 770 (8.19%) neonates, respectively, and 2) for multiple pregnancies 46 out of 77 (59.7%) and 22 out of 34 (64.7%) neonates, respectively.

Using linear regression analysis adjusted for maternal age and parity, we found that birth weight was significantly higher (340.4 g, R = 0.28) in neonates born after spontaneously conceived pregnancies than after ART. However, in singleton pregnancies only, there was no statistically significant difference in birth weight between the two groups. Furthermore, using Pearson's chi-square-test, there was no significant difference in the incidence of low-birth weight singletons (i.e., with birth weight <

2,500 g) between the two groups (i.e. ART vs spontaneous conception).

Neonatal Intensive Care Unit (NICU) hospitalization

Twelve singletons (12.9%) and 34 neonates from multiple pregnancies (50.7%) after ART were hospitalized in the NICU. Among children conceived spontaneously 78 singletons (10.1%) and ten from multiple pregnancies (29.4%) were hospitalized in the NICU. There were no perinatal deaths, neither in pregnancies after ART nor after spontaneous conception.

Using the chi-square test and independent samples t-test, we found that hospitalization of neonates in the NICU was more likely (χ^2-test; $p < 0.0001$) and lasted longer (independent samples t-test; $p < 0.0001$) in pregnancies after ART than after spontaneous conception. Conclusions were not altered after multiple regression analysis to adjust for maternal age, mode of delivery and parity (ANOVA, $p < 0.0001$). However, analysis in singleton pregnancies after exclusion of multiple pregnancies using the chi-square test and the independent samples t-test showed that hospitalization of neonates in the NICU was not significantly related with the mode of conception.

Discussion

In the present study, data from 913 consecutive pregnancies ending in live birth have been analyzed retrospectively, and obstetric and neonatal outcomes were compared between pregnancies after the use of assisted fertilization and spontaneous conception. This analysis showed that after use of ART cesarean section was more likely compared with pregnancies after natural conception. Exclusion of multiple pregnancies from this analysis did not alter conclusions. These findings are consistent with those of previous studies, which have shown that cesarean delivery rates were higher after ART, even in singleton pregnancies [6-8]. Management of pregnancies after assisted reproduction as high-risk pregnancies seems to be the main reason for the increased cesarean rates in such cases [5].

We also found that gestational age at birth and birth weight were lower following assisted fertilization as compared with pregnancies after spontaneous conception. However, exclusion of multiple pregnancies from this analysis showed that there were no significant differences in singletons, between the two groups. In other studies previously published [5-7, 9-17], gestational age at birth and birth weight were also lower after ART, even in singleton pregnancies.

Another finding in the present study was that hospitalization in the NICU was more likely in pregnancies after use of ART than after spontaneous conception. However, exclusion of multiple pregnancies from this analysis showed that in singletons there were no significant differences in days of hospitalization in the NICU between the two groups. These findings are in line with those of previous studies, suggesting that the iatrogenic increase in the rates of multiple pregnancies contributes to the relatively high neonatal morbidity in pregnancies after ART [4, 5, 7, 9, 10].

Conclusion

Our findings, consistent with those of previously published studies [4-17], show that in pregnancies after assisted fertilization there is a higher probability of cesarean section, lower gestational age at birth, lower birth weight and a higher risk of hospitalization in the NICU, than in pregnancies after natural conception. Though these findings have been observed in part even in singleton pregnancies, the iatrogenic increase of multifetal pregnancies appears to be the main contributing factor to the increase of these risks after assisted fertilization. Hence, with the implementation of single embryo transfer such problems could be reduced or even eliminated, without compromising the primary goal of providing healthy babies to infertile couples. Furthermore, besides improving neonatal morbidity, single embryo transfer could possibly decrease associated healthcare costs as well.

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