HHS Public Access

Author manuscript

Fertil Steril. Author manuscript; available in PMC 2016 January 05.

Published in final edited form as:

Fertil Steril. 2014 April ; 101(4): 1019–1025. doi:10.1016/j.fertnstert.2013.12.030.

Maternal characteristics and pregnancy outcomes after assisted reproductive technology by infertility diagnosis: ovulatory dysfunction versus tubal obstruction

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Abstract

Objective—To examine differences in maternal characteristics and pregnancy outcomes between women with ovulatory dysfunction (OD) and women with tubal obstruction (TO) who underwent assisted reproductive technology (ART).

Design—Retrospective cohort study.

Setting—Centers for Disease Control and Prevention.

Patient(s)—Exposed and nonexposed groups were selected from the 2000–2006 National ART Surveillance System linked with live-birth certificates from three states: Florida, Massachusetts, and Michigan.

Intervention(s)—None.

Main Outcome Measure(s)—Maternal characteristics and pregnancy outcomes, including newborn's health status right after delivery (Apgar score, <7 vs. ≥7) as the study outcome of interest, were assessed among women with OD/polycystic ovary syndrome (PCOS) and TO who used ART.

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The data were partially presented at the European Society of Human Reproduction and Embryology Annual Meeting, which was held in London, on July 7–10, 2013.

V.G. has nothing to disclose. Y.Z. has nothing to disclose. D.M.K. has nothing to disclose. E.S.-S. has nothing to disclose. M.S. has nothing to disclose. R.S.K. is a board member of the Perinatal Foundation (Wisconsin); a member of the pregnancy exposure registry scientific advisory committee of Amgen Corp.; and the primary investigator on several projects through the USF Birth Defects Surveillance Program, funded through the Centers for Disease Control and Prevention, the state of Florida, and the March of Dimes. H.D. has nothing to disclose. P.M. has nothing to disclose. D.J.J. has nothing to disclose.

Result(s)—A significantly higher prevalence of women with OD/PCOS were younger (<35 years of age; 65.7% vs. 48.9%), were white (85.4% vs. 74.4%), had higher education (29.4% vs. 15.6%), and experienced diabetes (8.8% vs. 5.3%) compared with those having TO. The odds of having a lower (<7) Apgar score at 5 minutes were almost twice as high among newborns of women with OD/PCOS compared with those with TO (crude odds ratio, 1.86; 95% confidence interval [CI], 1.31, 2.64; adjusted odds ratio, 1.90; 95% CI, 1.30, 2.77).

Conclusion(s)—Women with OD/PCOS who underwent ART have different characteristics and health issues (higher prevalence of diabetes) and infant outcomes (lower Apgar score) compared with women with TO.

Keywords

Ovulatory dysfunction (OD); polycystic ovary syndrome (PCOS); tubal obstruction (TO); assisted reproductive technology (ART); Apgar score

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As defined by the International Committee for Monitoring Assisted Reproductive Technology and the World Health Organization, “infertility is a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse” (1, 2). Worldwide, nearly 72.4 million couples experience fertility problems, with an incidence similar in most countries and independent of the level of the country’s development (3). According to 2006–2010 data from the National Survey of Family Growth (NSFG), in the United States, an estimated 6% of married women ages 15–44 years are infertile, and an estimated 11.9% (7.4 million) of women from the same age group have ever received infertility services (4). An estimated infertility prevalence of 15.5% was found in both married and cohabiting women 15–44 years of age by a recent study that used the same survey (NSFG) and a different novel current duration approach (5).

Infertility can have many causes and may be related to factors in the male, female, or both. In some cases, each partner may be independently fertile but the couple cannot conceive together without assistance (i.e., unexplained infertility) (6, 7). Risk behaviors and environmental exposure may also influence the ability to conceive (8).

One of the two most prevalent causes of female infertility is ovulatory dysfunction (OD), characterized by an impaired hormone profile that may have an impact on women’s health beyond and during pregnancy, assisted reproductive technology (ART) response, and pregnancy outcomes, including the offspring’s health. Chronic OD (i.e., oligo-ovulation, anovulation) is most commonly caused by polycystic ovary syndrome (PCOS), which is known for its hyperandrogenism, and disordered gonadotropin secretion (LH hypersecretion), which is often associated with insulin resistance (9–12). The syndrome, which modulates both hormonal and metabolic processes, is the most common endocrinopathy in reproductive-age women and increases women’s risk of infertility, cardiometabolic disease, and endometrial pathology (i.e., endometrial cancer) (13). PCOS is defined by any two of the following: clinical/ biochemical hyperandrogenism, OD, and polycystic ovaries (14, 15). PCOS most likely encompasses several distinct diseases with similar clinical phenotypes but different underlying pathophysiological processes. However,

hyperandrogenism remains the syndrome's clinical hallmark (13–15). The estimated prevalence of PCOS is between 6% and 10% based on the National Institutes of Health criteria and as high as 15% when the broader Rotterdam criteria are applied (14, 15). Its etiology remains obscure, and there is variability in phenotype expression, with evidence of a genetic component found in family and twin studies (16). When achieving pregnancy, women with PCOS have a significantly higher risk of developing gestational diabetes, pregnancy-induced hypertension, eclampsia, and preterm birth. The existing evidence suggests that PCOS has a life span pathway with two dimensions, horizontal (impact on women's health over time) and vertical (effects in offspring of women with PCOS shortly after delivery and over time due to fetal exposure to hyperandrogenism that might disturb epigenetic programming, in particular those genes regulating reproduction and metabolism) (16–18).

Conversely, tubal obstruction (TO), also known as tubal factor infertility, the second most common cause of female factor infertility, is a mechanical factor. Most commonly, tubes are obstructed owing to infection such as pelvic inflammatory disease (PID), with the rate of obstruction increasing after each episode of PID (8). Other infections that might occlude or disable the tubes include infections after childbirth or abortions and intra-abdominal infections including appendicitis and peritonitis. The hormone profile of women with TO alone should be relatively normal, assuming no impact on ovarian function due to previous surgeries or inflammation.

For over three decades, ART has been used in the United States to help women overcome infertility. The Centers for Disease Control and Prevention (CDC) has conducted surveillance on the use, efficacy, and outcomes of ART treatments in the United States since 1995 (19, 20). To promote state-based surveillance of ART and infertility, CDC's Division of Reproductive Health, in collaboration with the Florida Department of Health (FDOH), Massachusetts Department of Public Health (MDPH), and Michigan Department of Community Health (MDCH), formed the States Monitoring ART (SMART) Collaborative. SMART provides a unique opportunity for federal and state public health agencies to work together from linking the information from ART surveillance with state data (live births, infant and fetal deaths, other surveillance systems and registries) to conducting research. Thus far, this collaborative has focused on data validity and agreement, impact of ART on maternal health and pregnancy outcomes, and related trends. The linked files that have been created have not yet been used to assess the impact of different infertility diagnoses, independently of ART, on pregnancy characteristics and outcomes. As more linkages are performed, more information will be available and thus more studies may be designed with the scope of exploring and understanding infertility within the context of prior overall health of the reproductive-age population.

This paper examines the differences in maternal characteristics and pregnancy outcomes, including newborns' health immediately after birth, between women with the two most prevalent female-specific infertility diagnoses, OD and TO, who underwent ART procedures in the three states participating in the SMART Collaborative.

MATERIALS AND METHODS

We used the National ART Surveillance System (NASS) data linked with state live-birth records for the years 2000–2006 from Florida, Massachusetts, and Michigan and a retrospective cohort study design.

NASS is a web-based ART data collection system supported by the Division of Reproductive Health at CDC. The Fertility Clinic Success Rate and Certification Act of 1992 requires that all clinics performing ART provide data to the CDC annually for all initiated cycles during that year (20). NASS data cover >95% of ART cycles performed in the United States annually and include detailed information on each ART procedure (primarily IVF) performed during the reporting year (19). NASS contains information on reasons for performing each reported ART cycle (infertility diagnosis), which was used for the current analysis. The information on each ART procedure was collected from ART clinics by the Society for Assisted Reproductive Technology for the years 2000–2003 and by Westat for the years 2004–2006.

Data were linked with the three states' birth certificate files at CDC by using the CDC-developed software LinkPlus and a probabilistic linkage algorithm that led to identification of the live births resulting from ART (21). Maternal date of birth, infant date of birth, plurality, gravidity, and maternal resident ZIP codes by state were used as link factors. Ancillary variables used to solve questionable linkages included maternal race, infant birth weight, and infant sex. The linking success rates were 89.6 for Massachusetts, 90.1 for Florida, and 92.3 for Michigan. Two validation studies assessed the accuracy of the probabilistic linkage method and found high sensitivity and specificity (22).

Using the NASS female infertility diagnosis variables, we were able to limit our study to female-specific infertility, more specifically to women with only one of the following diagnoses: OD only (exposed) or TO only (nonexposed). There were no missing values in these variables. Women with PCOS make up the majority of the OD group (23); therefore, for the remainder of the study we will refer to women having ovulatory disorders as OD/PCOS and to those having tubal obstruction as TO. We also restricted the study to only the first successful ART delivery/birth for women identified as having multiple deliveries to thus focus on the study objectives and eliminate the potential impact of subsequent treatments on maternal complications and pregnancy outcomes.

The first part of the study focused on exploring the differences in selected maternal and pregnancy characteristics and in pregnancy outcomes including the newborn's immediate health between women with OD/PCOS (considered exposed to impaired hormone profile) and those with TO (considered nonexposed given the likelihood that this group has a normal hormone profile). Descriptive statistics were used, and percentages with their respective 95% confidence intervals (CIs) were reported.

The selected maternal and pregnancy characteristics, pregnancy outcomes, and newborn characteristics originated from the state live-birth records and included maternal age (<35 years; ≥35 years), race/ethnicity (white, black, Hispanic, other), education (high school degree and less, some college/college graduate, more than college), adequacy of prenatal

care (Kotelchuck index categories, ≥adequate, adequate, intermediate, and inadequate), comorbid conditions (preexisting hypertension, gestational hypertension, and diabetes that included both gestational and preexisting), delivery method (vaginal or cesarean section), induction of labor (yes or no), plurality (singleton, twins, and ≥triplets), gestational age at birth (<37 and ≥37 completed weeks gestation), birth weight (<2,500 and ≥2,500 g), pregnancy outcome (derived using a composite variable of gestational age and birth weight <37 completed weeks gestation and <2,500 g; ≥37 weeks gestation and ≥2,500 g), newborn sex (female or male), Apgar score at 5 minutes (<7 or ≥7), and neonatal intensive care unit (NICU) admission (yes or no). The last two variables were selected as measures of a newborn's health. The Apgar score, developed by Dr. Virginia Apgar, is a simple and repeatable method to quickly assess the newborn's health immediately after birth and to record fetal-to-neonatal transition, despite its limitations in preterm infants (24–26). NICU admission is often used as an indirect measure of the health status of preterm and low birth weight infants. Unfortunately, there was inconsistency in the reporting of this variable during the study period (Florida reported it from 2004) and therefore a high percentage of missing values.

In the second part of the study, we examined the impact of infertility diagnosis (impaired hormone profile in OD/PCOS compared with in TO) on the outcome of interest that was identified through bivariate analysis (crude odds ratios [cORs] and corresponding 95% CIs) of pregnancy outcomes and infant characteristics. With the intention to eliminate the impact of multiple pregnancies, and especially deliveries, on pregnancy outcomes and newborn characteristics, we restricted the analysis to only singletons and first-order multiples.

The association between OD/PCOS and the outcome of interest was explored further through multivariable analysis (logistic regression). The multivariable model was adjusted for maternal age, race, education, adequacy of prenatal care per the Kotelchuck index, comorbidities (hypertension and diabetes), method of delivery (vaginal and cesarean section), labor induction, composite gestational age and birth weight as pregnancy outcome, and infant's sex. Adjusted odds ratio (aOR) and 95% CI were reported for the outcome of interest.

SAS software version 9.2 and SAS callable SUDAAN version 10.0 (RTI International) were used for data analyses.

The project was approved by the Institutional Review Boards of CDC, FDOH, MDPH, and MDCH.

RESULTS

During 2000–2006, 16,876 women from Florida, Massachusetts, and Michigan underwent ART procedures that resulted in a live birth. Of these, 8.5% (n = 1,433) had infertility due to OD/PCOS only and 19.5% (n = 3,294) due to TO only.

Differences were observed between women with these two infertility diagnoses. Specifically, a significantly higher percentage of women with OD/PCOS were young (<35 years; 65.7%), white (85.4%), and more educated (more than college; 29.4%) compared

with women with TO (48.9%, 74.4%, and 15.6%, respectively). The prevalence of diabetes was significantly higher (8.8%) in women with OD/PCOS as compared with in women with TO (5.3%; Table 1). A significantly higher percentage of newborns of women with OD/PCOS had an Apgar score at 5 minutes that was below 7 (3.0%) compared with those born to women with TO (1.6%; Table 2).

In contrast, the prevalence of hypertension (preexisting and gestational) was not significantly different among women with OD/PCOS (31.3% and 33.6%, respectively) compared with those with TO (39.2% and 40.0%, respectively; Table 1). Also, no significant differences were found in adequacy of prenatal care, method of delivery and labor induction (Table 1), and pregnancy outcomes such as gestational age, birth weight, composite variable of the two, infant' sex. and NICU admissions (Table 2).

Bivariate analysis of selected pregnancy outcomes and infant characteristics of women with OD/PCOS compared with those with TO confirmed a significant difference between the two infertility groups in their respective Apgar scores at 5 minutes (<7 or ≥7; Table 2). Apgar score was therefore selected as the outcome of interest.

Multivariable modeling and analysis (logistic regression) revealed that the difference in Apgar score at 5 minutes remained statistically significant after controlling for maternal age, race, education, adequacy of prenatal care, comorbidities, method of delivery, labor induction, composite gestational age and birth weight, and infant's sex. Specifically, the odds of having an Apgar score <7 at 5 minutes was almost twice as high among newborns of women with OD/PCOS compared with among newborns of women with TO (Table 3).

DISCUSSION

The prevalence of OD/PCOS that was not associated with other infertility diagnoses among women from Florida, Massachusetts, and Michigan who underwent ART from 2000 through 2006 was 8.5%. It mirrors prior reports of PCOS prevalence among women of reproductive age (6%–10%) (14, 15). However, it is an underestimate of the true prevalence, given that only women who had OD/PCOS as their sole infertility diagnosis were counted. If we had included women with PCOS in conjunction with other causes of infertility, we would report the prevalence of PCOS as 11.7%.

When comparing women with OD/PCOS with those with TO, significant differences were found in the prevalence of certain maternal demographics, specifically age, race/ ethnicity, and education. The difference in age between the two groups may be partially explained by women with OD/ PCOS seeking infertility treatment earlier than their counterparts with TO owing to their ability to conceive spontaneously later in life. This is known as delayed fertile window in women with PCOS since there is a tendency to have regular menstrual cycles with advancing age (27). The high prevalence of white women in the OD/PCOS group compared with in the TO group is consistent with findings from other studies suggesting that ethnic origin and culture may contribute to the differing manifestation of infertility including PCOS (28). The race/ ethnic difference has also been highlighted at the European Society of Human Reproduction and Embryology/American Society for Reproductive Medicine–

sponsored Third PCOS Consensus Workshop that was held in 2010 (15). The high levels of education among women with OD/PCOS may reflect differences in socioeconomic status.

The significantly higher prevalence of diabetes found in our study among women with OD/PCOS compared with those having TO has been previously described (14, 15, 18). However, our study did not confirm some of the previously identified characteristics of women with PCOS, such as gestational hypertension (12, 17). The prevalence of multiple and preterm births were similar between women with OD/PCOS and women with TO, and no significant differences were observed in NICU admission rates, which are in contrast with other prior findings (29). The discrepancies that were found are likely due to the nature of our study population, which included only women who underwent ART, thus controlling for the procedure's impact on these particular characteristics and outcomes that may be stronger than those of the hormone profile alone, which was considered as exposure in our study.

The nonsignificant difference in low birth weight infants between the two infertility groups were found in other studies that suggested the possible impact the exposure to elevated androgen levels may have on a PCOS phenotype but with no impact on birth weight (30).

The significantly higher odds of lower Apgar score (<7) at 5 minutes in newborns of women with OD/PCOS reported by our study mirrors the findings of prior studies that explored the impact of PCOS on pregnancy outcomes and newborns (17, 29). Lower Apgar score within the context of a nonsignificant difference in NICU admission may reflect only a transient inability of newborns of women with OD/PCOS to adjust to the extrauterine environment due to abnormalities in placental steroidogenesis or other unknown reasons. This hypothesis is, in part, supported by the findings of a clinical study that measured and reported mixed cord blood T, androstenedione (A), dehydroepiandrosterone,17-hydroxyprogesterone, E_2, and dihydrotestosterone in newborns of women with PCOS compared with those hormone levels in the newborns of women with normal hormone profiles. In that study, the female offspring of women with PCOS were found to have lower cord blood A levels and E_2 levels that suggested decreased fetal or placental production of steroids due to an abnormality in placental steroidogenesis (31, 32). Despite being sex specific (female) and based on cord blood measurements that are not ideal for evaluation of prenatal androgen exposure, these findings may possibly explain the poor response of newborns of mothers with PCOS to labor and delivery stress and later to adjustment to the external environment, which are all reflected in a low Apgar score with or without admission to the NICU. Other explanations of the findings are, however, possible (29).

Unfortunately there are limited population-level data on PCOS available, and that could be the reason for limited penetration of the prior clinical study findings into the public health arena. The same limited penetration had the evidence related to familial aggregation of hormonal abnormalities in a study of first-degree relatives of women with PCOS and/ or the findings related to siblings of women with PCOS, including males, predisposed to hormonal abnormalities typical of PCOS (33–35). The increasing interest in linking clinical aspects with public health as well as in the knowledge related to fetal programming and familial aspects of chronic diseases set the perfect stage for improving the population-level

information on PCOS. Thus reproductive age–specific syndromes like PCOS may be incorporated within the priorities focused on chronic disease prevention and health promotion. Furthermore and perhaps the most important argument for the need for better data on and monitoring of PCOS for effective prevention strategies and public health actions is the high cost associated with this syndrome that has been estimated based on the knowledge gained thus far. For instance, given an estimated 4 million women of reproductive age (15–44 years) with PCOS in the United States (6.6% estimated prevalence), the annual economic burden is at least $4.36 billion. This estimate does not consider the greater frequency of pregnancy-related complications including gestational diabetes, preeclampsia, and miscarriage. Of note, the cost of the diagnostic evaluation accounted for a relatively minor part of the total costs (approximately 2%). Therefore, more widespread and liberal screening for the disorder appears be a cost-effective strategy, leading to earlier diagnosis and interventions followed by possible amelioration and prevention of serious sequelae (36). For the syndrome's management, emphasis may be placed on lifestyle and symptom-directed treatment until future new discoveries.

The major strength of our study is in its population-based approach with a large sample size of women in three states undergoing ART in multiple years. Another important strength is the use of a linked file, NASS with live-birth certificates, which provided access to maternal characteristics as well as to pregnancy and newborn outcomes that are unavailable in NASS. Our study is also unique in that exposed and nonexposed groups were selected from the same cohort of women who underwent ART. More specific, women with TO provide an appropriate nonexposed group owing to their difference in hormone profiles compared with women with OD/PCOS and not in terms of fertility treatment, since women from both groups underwent ART. Thus the study findings mainly reflect the impact of the impaired hormone profile of PCOS (exposure) on maternal and pregnancy characteristics and furthermore on the selected outcomes of interest. To our knowledge, this study is the first to assess the impact of different infertility diagnoses, independently of ART, on pregnancy characteristics and outcomes by using the linked files created through the SMART collaborative.

There are, however, a few limitations to acknowledge. First, information about preexisting conditions and even gestation-related health issues could be incomplete in the live-birth records. For example, underreporting and thus missing values prevented us from exploring gestational diabetes separately. Second, we were not able to use the NICU admission rate in multivariate analysis since the information is not available in all three states. Nevertheless, our study findings from Florida and Michigan mirrored existing knowledge regarding the effects of PCOS on pregnancy outcomes and newborns' health status shortly after birth (17). Another gap in the data that were available was the women's weight, which is a known risk factor among women with PCOS that we were unable to account for due to a lack of data available in the live-birth files from all three states. Women with PCOS have an increased propensity towards OD in the presence of obesity, with anovulatory patients with PCOS having a greater body mass index than their ovulatory sisters, despite both siblings having ovarian hyperandrogenism (37, 38). Adverse outcomes in women with PCOS might be exacerbated by obesity.

In conclusion, women/mothers with OD/PCOS who underwent ART have different maternal and pregnancy issues (high prevalence of diabetes) and offspring outcomes (lower Apgar score) compared with women with TO. Prevention strategies targeted towards improving the metabolic and endocrine consequences of OD/PCOS, such as changes in lifestyle, diet, and appropriate vitamin supplementation may optimize the health of women with the syndrome before conception (39–41). Assessing whether a woman has a family history of PCOS and evaluating her risks during pregnancy and postpartum as well as her newborn's health status may lead to targeted prevention strategies that in turn may decrease both the health risks and economic burden of PCOS.

There is an increasing awareness that PCOS is a condition associated with an increased morbidity and long-term health problems beyond infertility (17). The population-based approach of our study adds value to the existing body of literature related to PCOS and warrants further consideration of public and private collaboration for better data collection and monitoring.

Acknowledgments

The authors thank Dr. Maurizio Macaluso for initiating the SMART collaborative.

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TABLE 1

Maternal and pregnancy characteristics by specific infertility diagnosis (OD/PCOS and TO)—2000–2006 NASS data linked with state live-birth records from Florida, Massachusetts, and Michigan.

	OD/PCOS (only)		TO (only)	
	n	**Percent (95% CI)**	**n**	**Percent (95% CI)**
Total	1,433	100.0 (8.5% of 16,876)	3,294	100.0 (19.5% of 16,876)
Age				
<35	941	65.7 (62.7, 68.5)	1,611	48.9 (45.1, 52.7)
≥35	492	34.3 (31.5, 37.3)	1,683	51.1 (47.3, 54.9)
Missing/unknown[a]	0		0	
Race/ethnicity				
White	1,224	85.4 (80.6, 89.2)	2,451	74.4 (69.2, 79.0)
Black	23	1.6 (1.1, 2.3)	281	8.5 (7.1, 10.2)
Hispanic	76	5.3 (2.5,11.0)	374	11.4 (7.2, 17.4)
Other[b]	97	6.8 (5.4, 8.5)	160	4.9 (3.7, 6.3)
Missing/unknown[a]	13	0.9	28	0.9
Education				
High school and less	151	10.5 (8.7, 12.7)	884	26.8 (24.2, 29.7)
Some college/college graduate	854	59.6 (55.8, 63.3)	1,866	56.6 (54.5, 58.8)
More than college	421	29.4 (26.5, 32.4)	514	15.6 (13.7, 17.7)
Missing/unknown[a]	7	0.9	30	0.9
Adequacy of prenatal care				
Adequate+	838	58.5 (55.7, 61.2)	1,839	55.8 (53.9, 57.7)
Adequate	422	29.4 (26.5, 32.6)	1,039	31.5 (29.8, 33.3)
Intermediate	80	5.6 (4.2, 7.4)	194	5.9 (4.5, 7.6)
Inadequate	28	2.0 (1.4, 2.8)	67	2.0 (1.6, 2.5)
Missing/unknown[a]	65	4.5	155	4.7
Comorbid condition[c]				
Preexisting hypertension	449	31.3 (17.9, 48.9)	1,291	39.2 (22.3, 59.1)
Gestational hypertension	481	33.6 (21.0, 49.0)	1,319	40.0 (24.3, 58.2)
Diabetes (gestational and preexisting)	126	8.8 (6.7, 11.4)	176	5.3 (4.5, 6.4)
Missing/unknown[a]	82	5.7	80	2.4
Plurality				
Singletons	929	64.8 (62.0, 67.6)	2,179	66.2 (63.7, 68.5)
Twins	461	32.2 (29.8, 34.6)	1,021	31.0 (28.7, 33.4)
≥Triplets	43	3.0 (2.2, 4.0)	94	2.9 (2.2, 3.7)
Missing/unknown[a]	0		0	
Delivery method				
Vaginal	674	47.0 (43.7, 50.4)	1,545	46.9 (44.4–49.4)
Cesarean section	754	52.6 (49.2, 56.0)	1,742	52.9 (50.4–55.4)
Missing/unknown[a]	5	0.3	7	0.2

	OD/PCOS (only)		TO (only)	
	n	**Percent (95% CI)**	**n**	**Percent (95% CI)**
Labor induction				
Yes	193	13.5 (10.1, 17.7)	412	12.5 (10.5, 14.8)
No	936	65.3 (57.1, 72.7)	2,039	61.9 (50.9, 71.8)
Missing/unknown[a]	304	21.2	843	25.6

Note: Male infertility is not included.

[a] We did not consider it necessary to provide the 95% CI for missing/unknown.

[b] Massachusetts provided only four levels.

[c] Not mutually exclusive and including only women with at least one of the comorbid conditions of interest.

TABLE 2

Pregnancy outcomes and newborn characteristics among singleton births and first-order multiples, by infertility causes—2000–2006 NASS data linked with state live-birth records from Florida, Massachusetts, and Michigan.

	OD/PCOS (only)		TO (only)		
	n	**Percent (95% CI)**	**n**	**Percent (95% CI)**	**cORs (95% CI)**
Total	1,433	100.0 (8.5% of 16,876)	3,294	100.0 (19.5% of 16,876)	
Gestational age					1.09 (0.98, 1.22)
<37 weeks	455	31.8 (29.7, 33.9)	984	29.9 (27.6, 32.3)	
≥37 weeks	971	67.8 (65.8, 69.6)	2,293	69.6 (67.3, 71.8)	
Missing/unknown[a]	7	0.5	17	0.5	
Birth weight					1.10 (0.98, 1.24)
<2,500 g	382	26.7 (24.3, 29.1)	818	24.8 (23.1, 26.7)	
≥2,500 g	1,046	73.0 (70.6, 75.3)	2,469	75.0 (73.1, 76.7)	
Missing/unknown[a]	5	0.3	7	0.2	
Composite variable (gestational age and birth weight)					1.14 (1.00, 1.31)
<37 weeks and <2,500 g	332	23.2 (20.9, 25.6)	679	20.6 (18.8, 22.5)	
≥37 weeks and ≥2,500 g	925	64.5 (62.5, 66.6)	2,163	65.7 (63.3, 67.9)	
Otherwise	167	11.7 (10.2, 13.3)	433	13.1 (12.0, 14.4)	
Missing/unknown[a]	9	0.6	19	0.6	
Infant sex					1.12 (0.99, 1.27)
Male	738	51.5 (48.6, 54.4)	1,790	54.3 (52.6, 56.0)	
Female	695	48.5 (45.6, 51.4)	1,504	45.7 (44.0, 47.4)	
Missing/unknown	0		0		
Apgar score					1.86 (1.31, 2.64)
<7	43	3.0 (2.3, 3.9)	54	1.6 (1.2, 2.1)	
≥7	1,385	96.7 (95.8, 97.3)	3,232	98.1 (97.6, 98.5)	
Missing/unknown[a]	5	0.3	8	0.2	
NICU admission					1.19 (0.97, 1.47)
Yes	279	19.5 (16.0, 23.5)	504	15.3 (11.7, 19.8)	
No	921	64.3 (58.0, 70.1)	1,985	60.3 (49.8, 69.9)	
Missing/unknown[a]	233	16.3	805	24.4	

[a] We did not consider it necessary to provide the 95% CI for missing/unknown.

TABLE 3

Crude and adjusted ORs[a] of Apgar score below 7 in offspring of women with OD/PCOS versus those with TO —2000–2006 NASS data linked with state live-birth records from Florida, Massachusetts, and Michigan.

	cOR (95% CI)	aOR[a] (95% CI)
OD/PCOS	1.86 (1.31, 2.64)	1.90 (1.30, 2.77)
TO	1.0	1.0

[a]We controlled for maternal age, race, education, adequacy of prenatal care per the Kotelchuck index, comorbidities (hypertension and diabetes), method of delivery (vaginal and cesarean section), labor induction, composite gestational age and birth weight as pregnancy outcome, and infant's sex.