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

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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.

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. (Fertil Steril® 2014;101:1019–25. ©2014 by American Society for Reproductive Medicine.)

Key Words: 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