Adverse obstetric and perinatal outcomes in subfertile women conceiving without assisted reproductive technologies

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Objective: To determine whether adverse perinatal outcomes are increased in subfertile women.
Design: Cohort study.
Setting: Two tertiary assisted reproductive technologies (ART) centers; Victorian births register.
Patient(s): Records of women who registered with the clinics (1991–2000), but did not have an infant using ART, were linked to the birth register (1991–2004) to identify singleton non-ART births within 5 years of registration (N = 2171). Controls, matched by maternal age and year of infant's birth, were selected randomly from birth records (N = 4363).
Interventions: None.
Main Outcome Measure(s): Adverse obstetric and perinatal outcomes.
Result(s): After adjusting for confounders, compared with controls, subfertile women had increased odds of hypertension or preeclampsia (adjusted odds ratio [OR] 1.29, 1.02–1.61), antepartum hemorrhage (adjusted OR 1.41, 1.05–1.89), perinatal death (adjusted OR 2.19, 1.10–4.36), low birth weight (adjusted OR 1.44, 1.11–1.85), preterm birth <37 weeks (adjusted OR 1.32, 1.05–1.67) or <31 weeks (adjusted OR 2.37, 1.35–4.13), and cesarean delivery (adjusted OR 1.56, 1.37–1.77). There was weak evidence for increased birth defects (adjusted OR 1.30, 0.98–1.72) and gestational diabetes (adjusted OR 1.25, 0.96–1.63). No increased risk was found for prelabor rupture of membranes, small for gestational age, or postpartum hemorrhage.
Conclusion(s): Subfertile women with singleton births are at increased risk of several adverse outcomes. These risks should be considered during their antenatal care and when analyzing adverse effects of ART. (Fertil Steril® 2010;94:2674–9. ©2010 by American Society for Reproductive Medicine.)

Key Words: Subfertility, complications of pregnancy, preterm birth, low birth weight, birth defects, preeclampsia, antepartum hemorrhage

Many studies have linked adverse obstetric and birth outcomes with assisted reproductive technologies (ART) (reviewed by Halliday [1]). Whether the ART procedures or factors associated with the infertility contribute to the adverse outcomes has been investigated with conflicting results (2–6). Some suggest that they are specific adverse effects of ART, which lead to adverse perinatal outcomes (7–9). Others conclude that the laboratory procedures involved with IVF could not be responsible and that they are related to the health of the infertile woman (5, 6). This latter view is supported somewhat by studies of subfertility, defined in different studies as a previous diagnosis of infertility or a prolonged time to pregnancy, showing increased risk of preterm birth (10–15), cesarean section (11, 14), low birth weight (11, 14), pregnancy-induced hypertension or preeclampsia (11, 14), perinatal death (16), and birth defects (17) after conception without ART. The aims of this study were to compare the prevalence of adverse obstetric and singleton birth outcomes between subfertile women and women from the general population (controls).

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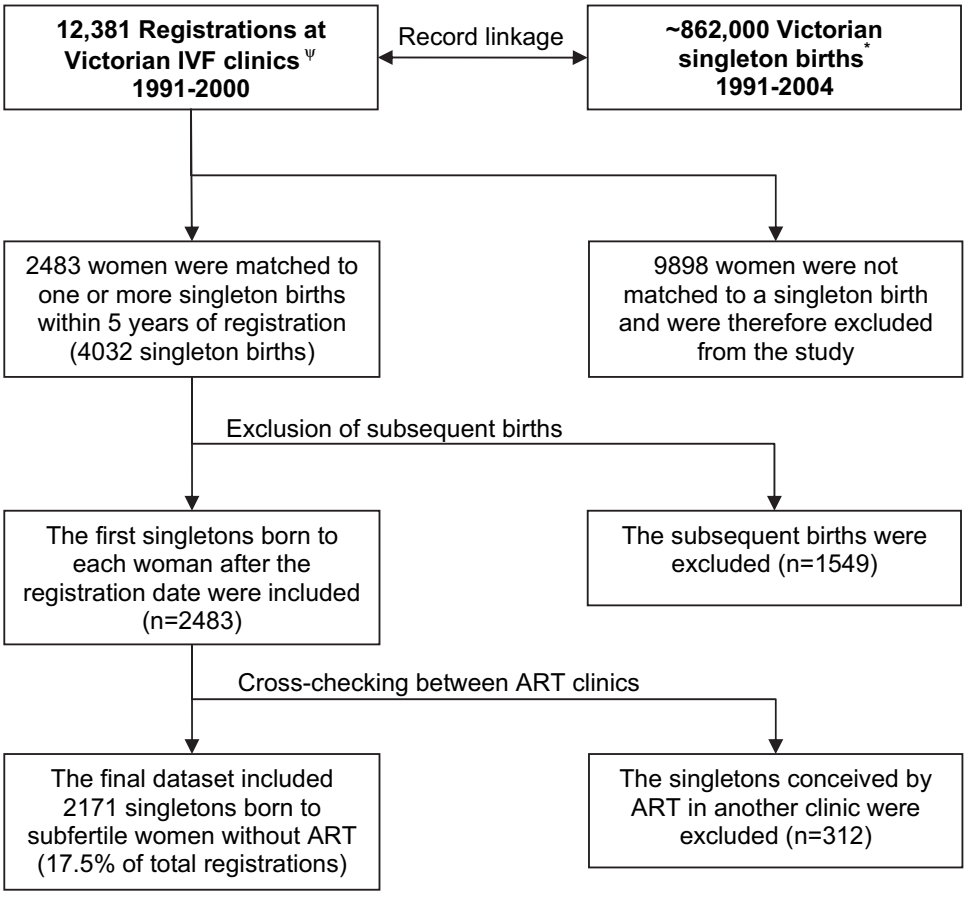
FIGURE 1

Flow diagram of the record linkage process between IVF registration data and perinatal birth data.



Ψ Women who registered at Monash IVF and/or Melbourne IVF, but who did not achieve an ongoing pregnancy through ART

* Victorian singleton births are those born at 20 weeks gestation and over

Jaques. Birth outcomes with subfertility. Fertil Steril 2010.

MATERIALS AND METHODS

Subfertile Women

For the purposes of this study, a subfertile woman is defined as a woman who registered at a clinic for infertility and went on to conceive and give birth to a singleton infant without ART. All 12,381 women who registered at either or both of the major ART clinics (Monash IVF or Melbourne IVF) in Victoria between 1991 and 2000 but who did not conceive with IVF, intracytoplasmic sperm injection (ICSI), GIFT, or artificial insemination with husband or donor sperm, were linked to the Victorian birth data between 1991 and 2004 (Fig. 1). Women who registered in any given year were followed up for birth in that year and the subsequent 4-year period. During 1991 to 2000 there were four ART clinics in Victoria, but Monash IVF and Melbourne IVF treated more than 90% (93.7% in 2000) of the women (18). Only the first singleton birth in the study period was considered. All multiple births were excluded from the study. By focusing on singleton births, we avoided the complexity of disentangling the recognized perinatal problems associated with twin and higher order pregnancies from those potentially attributable to the underlying subfertility.

Databases for Record Linkage

1. Assisted reproductive technologies clinic databases: The databases included clinical features, diagnosis, and treatments for some subjects. Additional information about diagnostic investigations and lifestyle factors was sought from the patients' records, but many patients, particularly those who conceived quickly, had incomplete investigations.
2. Victorian birth data: The Perinatal Data Collection Unit (PDCU), Department of Human Services, oversees mandatory registration of all births of 20 weeks gestation and over. Stillbirths and neonatal deaths are registered; miscarriages (<20 weeks gestation) are not. Information about preexisting health, previous pregnancies, maternal complications of pregnancy and birth, gestation at birth, and infant's weight and sex are recorded by midwives on a standard birth form. There were approximately 862,000 singleton births from1991 to 2004. More than 99.6% of all births in Victoria were reported to the PDCU in 1995 (19).
3. Victorian Birth Defects Register: This is also held at the PDCU with mandatory notification of birth defects on the birth form including data on terminations at all gestations. This data set has additional voluntary notifications from multiple sources in infants and children up to 15 years of age. There are approximately 2,500 birth defects reported per year in Victoria (4% of all births). Audits before 2004 indicate