

Impact of assisted reproductive technology on the incidence of multiple-gestation infants: a population perspective

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Objective: To study the value of a population view in assessing assisted reproductive technology (ART) multiple-gestation infants.
Design: Descriptive comparison of ART treatment and population statistics in seven developed countries (United States [U.S.], South Korea, United Kingdom, the Netherlands, Australia, Belgium, Denmark) with varying ART utilization and single-embryo transfer (SET) rates.

Setting: Not applicable.

Patient(s): Not applicable.

Intervention(s): None.

Main Outcome Measure(s): The contribution of ART multiple-gestation infants to the total number of multiple-gestation infants in a population was calculated in relation to utilization of ART and SET rates.

Result(s): The number of ART treatments leading to embryo transfer varied from 304 per million inhabitants in the U.S. to 1,518 in Denmark. The percentage of ART cycles that utilized SET varied from 8.8% in South Korea to 53.3% in Australia. Reflecting both utilization rates and SET rates, the percentage of multiple-gestation infants in the population attributed to ART ranged from 14.7% in South Korea to 29.0% in Denmark.

Conclusion(s): In seven countries, the contribution of ART multiple-gestation infants to all multiple-gestation infants varies from 14.7% to 29.0%, a percentage that was influenced by both the SET rate per cycle and ART utilization rates. In the monitoring of safety and efficacy of fertility treatment, registration of the percentage of SET cycles alone might not be sufficient. (Fertil Steril® 2015;103:179–83. ©2015 by American Society for Reproductive Medicine.)

Key Words: Single-embryo transfer, multiple pregnancies, assisted reproductive technology, outcome measure

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The ultimate goal of fertility treatment is to achieve the birth of a healthy child in couples needing

medical assistance to bear children. Particularly until the past decade, one commonly used approach to increase

the chance of success of assisted reproductive technologies (ARTs) was to transfer multiple embryos (1). This approach resulted in improved pregnancy rates but also increased the risk of multiple pregnancies. The large number of multiple pregnancies occurring after ART treatment became a cause for concern, because multiple pregnancies are associated with an increase in maternal and perinatal

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morbidity and mortality as well as high health care costs (2–6).

Gerris et al. (7) was the first to report that single-embryo transfer (SET) could prevent multiple pregnancy, and SET is now widely accepted as best practice for minimizing the risk associated with multiple pregnancies (8, 9). Furthermore, in association with an effective cryopreservation program, SET has been shown to achieve cumulative live birth rates similar to double-embryo transfer (10–14).

In view of these developments, it has been suggested that the percentage of SET cycles should be used as a quality indicator for ART, along with expressions of success based on pregnancy or live birth rates (15). The shift to SET, however, has occurred at a time of increasing utilization of ART worldwide, with annual increases of 5%–10% in most countries over the past decade (16–19). Although it is clear that SET in the majority of patient groups is the best way to reduce the multiple birth rate from a patient perspective, it is also observed that after a number of failed ART cycles, couples switch to the use of double-embryo transfer. This phenomenon could then, together with the increase of ART utilization, partly undo the reduction of multiple pregnancies that is obtained from SET.

Because there are considerable differences existing in both SET and ART utilization rates among countries, the purpose of the present study was to investigate the association among ART utilization, SET rates, and the contribution of ART multiple-gestation infants to population multiple-gestation infant rates.

METHODS

Data Collection

We studied ART data from the United States (U.S.), South Korea, United Kingdom (U.K.), the Netherlands, Australia, Belgium, and Denmark. These countries have different policies regarding the indications, reimbursement, and clinical practice of ART treatment, resulting in both significant differences in SET and ART utilization rates (20). For example, in the U.K., treatment is primarily offered through private clinics and funded directly by patients, whereas in the Netherlands, treatment is primarily offered through general and university hospitals and funded by insurance companies. Previously, type of funding proved to influence the implementation of SET in the U.K. compared with Australia, where there is a more supportive approach toward funding ART and SET was better implemented (8).

For each of the seven countries, we collected information on the number of ART cycles resulting in fresh embryo transfer, the number of SET cycles, and the outcome of ART (number of live births, numbers of live born singletons, live born children in twin pregnancy, and live born children in high-order multiple pregnancies). For each country we collected information on the number of inhabitants, the number of all live born children from singleton, twin, and high-order multiple pregnancies, and the mean female age at the birth of the first child.

In this manuscript, ART cycles refer to IVF cycles and ICSI cycles. The numbers of autologous ART cycles undertaken in

2006 were taken from national registries, as were the outcomes of those cycles (21–23). Population statistics were obtained from national statistics bureaus in each country (24–30).

We used cross-sectional data for ART treatments performed in 2006 and population denominators of all infants born in 2006. That year was chosen because the potential impact of SET was already known and wide discrepancies existed in ART utilization and SET rates. Therefore, treatment data from 2006 provided an opportunity to investigate the impact that differences in ART utilization and SET rates had on ART's contribution to population multiple birth rates.

ART Outcome and General Population

Outcome measures were: 1) the number of fresh cycles leading to embryo transfer per million inhabitants; 2) the SET rate for fresh embryo transfer cycles; 3) the ART multiple-gestation infant rate resulting from all ART cycles; 4) the percentage of infants conceived after ART out of all infants born a population; and 5) the percentage of ART multiple-gestation infants out of all multiple gestation infants born in a population. A multiple-gestation infant was defined as a live born child out of a twin or high-order multiple pregnancy. Institutional Review Board approval was not obtained because this manuscript used only free, accessible, anonymous data.

RESULTS

Demographics

Table 1 presents the characteristics of the populations that were studied. The mean age at which women delivered their first child was 28 years, with the U.S. (mean 25 years) and U.K. (mean 30 years) at the extremes. The percentage of live born children compared with the absolute number of women of reproductive age (15–49 years) in 2006 varied from 3.4% in South Korea to 5.8% in the U.S.

ART Utilization

The utilization of ART differed widely among the selected developed countries. Three countries exhibited relatively high utilization (Denmark, Belgium, and Australia), and three countries exhibited relatively low utilization (U.S., U.K., and South Korea). The countries with the highest utilization were Denmark and Belgium, with 1,518 and 1,349 fresh embryo transfers per million inhabitants, respectively, whereas the U.S. and the U.K. recorded rates of 304 and 486 fresh embryo transfers per million inhabitants (Table 1).

The Use of Single-embryo Transfer

The use of SET also varied widely among the countries. The three countries with high ART utilization exhibited high SET rates, and the reverse was true for the three countries with low ART utilization rates. Belgium, Denmark, and Australia recorded SET rates of 49.2%, 36.4%, and 53.3% of fresh embryo transfers, respectively, whereas the U.K., the U.S., and South Korea recorded SET rates of 11.6%, 10.7%,

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