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## Access to Infertility Treatment Influences Outcomes

BY PATRICE WENDLING

ATLANTA — Access to infertility treatment influences utilization rates but also changes outcomes, including high-order multiple births, research suggests.

Investigators used data collected from 2000 to 2004 from 54 countries through the International Committee Monitoring Assisted Reproductive Technologies (IC-MART) to determine how economic factors influence the risk and benefit decisions made by providers and patients.

They found that assisted reproductive technology (ART) is used most frequently in societies that recognize infertility treatment as a reproductive right and consequently provide free access to treatment. When ART is funded out of pocket, it reaches only a small proportion of infertile couples, Dr. Fernando Zegers-Hochschild, ICMART vice chair, said at the annual meeting of the American Society for Reproductive Medicine (ASRM).

An estimated 64% of presumably infertile women requiring ART, aged 20-44 years, have access to ART treatment in Israel, where reimbursement is among the most generous in the world. This compares with 40% in Denmark and 32% in Australia, where cycles are free or reimbursed, and just 7% in the United States, where reimbursement is nil or limited.

In 2004, there were 1,083-2,000 ART cycles for every million inhabitants in Israel, Denmark, and Australia, while in the United States, there were only 357 cycles per million people. The number of ART cycles fell to just 50-150 cycles per million people in developing Latin American countries without reimbursement.

When ART is funded out of pocket, more embryos are transferred in order to achieve pregnancy with fewer attempts, generating an excess of twins and highorder multiple births, Dr. Zegers-Hochschild said. The financial motivation is not surprising, given the roughly \$15,000 price tag per ART cycle. Financial pressure from patients and publication of performance data also are driving competition for high success rates and the transfer of more embryos.

In 2004, 67% of transfers in Sweden were single-embryo transfers, and the remaining 33% were two-embryo transfers. In contrast, 8% of transfers in the United States that year involved one embryo; 40%, two embryos; 32%, three embryos; and 20%, four or more embryos.

During the same year, the twin and high-order multiple birth rates in Sweden were 5.6% and 0.1% vs. 30.4% and 1.1% in the United States, the latter down from 4.3% in 2000. Part of the reduction in the U.S. triplet rate has been achieved through the use of embryo reduction, which is not reported by the Centers for Disease Control and Prevention, said Dr. Zegers-Hochschild of the unit of reproductive medicine, Clinicas las Condes, Santiago, Chile.

This relationship between access and infertility treatment outcomes is also

present within countries. In a separate presentation at the same meeting, Yale University investigators in New Haven, Conn., led by Dr. J. Ryan Martin, reported that the number of embryos transferred per cycle, cancellation rate, twin rate, and multiple live birth rate were all significantly higher in states that did not mandate insurance coverage for in vitro fertilization (IVF). Only six states mandate coverage of two or more IVF cycles: Connecticut, Illinois, Massachusetts, Maryland, New Jersey, and Rhode Island.

Single-embryo transfer (SET) policies are being considered in several states to reduce multiple births, notably in California where residents are wrestling with the cost of premature octuplets born to "octomom" Nadya Suleman after she had six embryos transferred during infertility treatment. SET mandates have been put in place in countries like Belgium, with the potential cost savings from neonatal care of premature ART babies used to help fund infertility treatment, Dr. Zegers-Hochschild said in an interview.

Although ASRM immediate past president and fellow ICMART officer Dr. David Adamson agreed that the U.S. twin and triplet rates need to be reduced, he urged caution regarding SET mandates.

"This is very complicated medicine," he said in an interview. "The delivery rate per retrieval in the United States is

almost 50% better than in other countries. So, how much do you bring down the success rate to limit poor outcomes or complications?"

Evoking across-the-board regulations would interfere with the physician's ability to treat patients individually and does not address what happens if treatment fails. For example, ART treatment is reimbursed in Sweden, but if the treatment fails, a woman has to go back to the end of the line and possibly wait a year for another cycle, said Dr. Adamson, an ob.gyn. who specializes in reproductive endocrinology and infertility in Palo Alto, Calif. This can have devastating consequences, particularly for older women, and has prompted increasing use of private infertility clinics and personal financing.

"It must be a balance of risks and benefits," Dr. Adamson said. "It is a decision of complexity that should be left to the physician and patient. And, professional guidelines must be followed."

In October 2009, ASRM and the Society for Assisted Reproductive Technology issued new embryo transfer guidelines that "consideration should be given to transferring only a single embryo" for patients under age 35 who have a favorable prognosis, and recommended transferring only one more embryo than called for in four age-based prognostic categories. The number of embryos recommended for transfer increases with age ("Embryo Transfer Guidelines

Tightened," November, 2009, p. 1).

The societies also encourage individual fertility programs to generate and use their own data regarding patient characteristics and the number of embryos to be transferred. The ICMART database contains data from 54 countries, including 26 in which 100% of clinics reported their outcomes. In 2004 there were 724,247 ART cycles, up 53% from 475,054 in 2000, resulting in 132,809 deliveries and 165,278 babies.

Although the socioeconomic aspects of ART utilization are intricate and unique to each country, both Dr. Adamson and Dr. Zegers-Hochschild agreed that society needs to first recognize infertility as a public health issue if reimbursement and outcomes are to improve. The World Health Organization has recognized infertility as a public health issue and as a disease in its recently revised glossary of ART terminology developed with ICMART (Fertil. Steril. 2009;92:1520-4). (See related article, p. 11.) The CDC recognizes infertility as a public health issue, but not yet as a disease, Dr. Adamson said.

Disclosures: Dr. Zegers-Hochschild disclosed no conflicts of interest. Dr. Adamson reported receiving funding from EMD Serono Inc., Institute Biochimique SA, and LabCorp.

## **Study Shows Patient Support for Single-Egg IVF Transfer**

The majority of patients were supportive of a mandatory single-blastocyst transfer policy in a survey of 262 infertile women.

The idea of mandating single-blastocyst transfer during infertility treatment is being debated in several states following the widely publicized case of Nadya Suleman and her octuplets, but also raises concerns that such policies don't provide the flexibility needed to treat individual patients.

The anonymous 50-question survey was conducted between September 2008 and May 2009 at the University of Iowa after 2003 implementation of a mandatory single-blastocyst transfer policy at the university for women aged 38 years and younger with no history of failed in vitro fertilization who also had at least seven fertilized oocytes and one good-quality blastocyst on the day of transfer.

Overall, 94% of patients were supportive on some level of the mandatory policy, Sarina Martini reported at the meeting. The level of support on a 4-point scale ranged from 25% being "extremely" supportive; 42%, "supportive"; 27%, "somewhat" supportive; and 6%, "not at all" supportive.

Support for the mandatory policy was not significantly different in women who qualified for the policy

versus those who did not. Of the 262 women surveyed, 99 (38%) could transfer only one embryo.

Personal or societal concern about multiple-gestation pregnancy was the only significant predictor of support in an analysis that also included age, level of education, parity and gravidity, embryos in storage, children at home, previous in vitro fertilization/embryo transfers, failed transfers, duration of infertility, and insurance coverage.

The mean age of the women was 33 years, 86% had a college education or higher, 97% were married, 40% were nulliparous, and 42% had less than 20% insurance coverage for in vitro fertilization. Only 25% had been infertile for more than 5 years.

Overall, 87% of women felt that they had the right amount of input regarding the number of embryos to be transferred versus 13% who felt it was not enough, said Ms. Martini, a medical student at the University of Iowa in Iowa City. When asked specifically how much input they had in deciding the number of embryos transferred, 35% of women said they had no input; 14%, "a little" input; 20%, "moderate" input; and 31%, "a lot" of input.

The mean number of embryos transferred was 1.6, and the median

was 2. In all, 71% were fresh transfers, and 29% were cryopreserved.

The mandatory transfer policy is for fresh transfers only, and is coupled with a standardized educational summary on the comparative risks of multiple versus singleton pregnancies to maternal and child health, Ms. Martini said. The policy has not affected ongoing pregnancy rates, which have been maintained at 55%-60%, while multiple pregnancies have been significantly reduced from 40% in 2003 to 10% in 2007.

Audience members seemed eager for details on the educational materials, with one physician remarking that his clinic in Tampa has had little success with a voluntary policy offering women a subsequent frozen embryo transfer free of charge if they agree to initial single-embryo transfer. Others questioned if the survey responses could have been influenced by a partner, to which Ms. Martini responded that all but one or two patients completed the survey with the assistance of a nurse and had partners in the waiting room. The investigators plan to follow the patients to see if attitudes change over time.

**Disclosures:** The authors reported no conflicts of interest.