ORIGINAL ARTICLE: ENVIRONMENT AND EPIDEMIOLOGY

Intracytoplasmic sperm injection use in states with and without insurance coverage mandates for infertility treatment, United States, 2000–2015

Ada C. Dieke, Dr.P.H., M.P.H.,[a,b] Akanksha Mehta, M.D., M.S.,[b,c] Dmitry M. Kissin, M.D., M.P.H.,[b] Ajay K. Nangia, M.B.B.S.,[d] Lee Warner, Ph.D., M.P.H.,[b] and Sheree L. Boulet, Dr.P.H., M.P.H.[b]

[a] Epidemic Intelligence Service, Division of Scientific Education and Professional Development, Center for Surveillance, Epidemiology and Laboratory Services, Centers for Disease Control and Prevention, Atlanta, Georgia; [b] Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia; [c] Department of Urology, Emory University School of Medicine, Atlanta, Georgia; and [d] Department of Urology, University of Kansas Medical Center, Kansas City, Kansas

Objective: To compare indications and trends in intracytoplasmic sperm injection (ICSI) use for in vitro fertilization (IVF) cycles among residents of states with and without insurance mandates for IVF coverage.
Design: Cross-sectional analysis of the National Assisted Reproductive Technology Surveillance System from 2011 to 2015 for the main outcome and from 2000 to 2015 for trends.
Setting: IVF cycles performed in U.S. fertility clinics.
Patient(s): Fresh IVF cycles.
Intervention(s): Residency in a state with an insurance mandate for IVF (n = 8 states) versus no mandate (n = 43 states, including DC).
Main Outcome Measure(s): ICSI use by insurance coverage mandate status stratified by male-factor infertility diagnosis.
Result(s): During 2000–2015, there were 1,356,377 fresh IVF cycles, of which 25.8% (n = 350,344) were performed for residents of states with an insurance coverage mandate for IVF. ICSI use increased significantly during 2000–2015 in states both with and without a mandate; however, for non–male-factor infertility cycles, the percentage increase in ICSI use was greater among nonmandate states (34.6% in 2000 to 73.9% in 2015) versus mandate states (39.5% in 2000 to 63.5% in 2015). For male-factor infertility cycles, this percentage increase was ~7.3% regardless of residency in a state with an insurance mandate for IVF. From 2011 to 2015, ICSI use was lower in mandate versus nonmandate states, both for cycles with (91.5% vs. 94.5%), and without (60.3% vs. 70.9%) male-factor infertility.
Conclusion(s): Mandates for IVF coverage were associated with lower ICSI use for non–male-factor infertility cycles. (Fertil Steril® 2018;■:■–■. ©2018 by American Society for Reproductive Medicine.)
Key Words: Intracytoplasmic sperm injection, male infertility, insurance mandate, infertility, assisted reproductive technology

Discuss: You can discuss this article with its authors and other readers at https://www.fertstertdialog.com/users/16110-fertility-and-sterility/posts/28869-25038

Intracytoplasmic sperm injection (ICSI), an assisted reproductive technology (ART) procedure where a single sperm is injected directly into a mature egg, is indicated for the treatment of male-factor infertility when sperm parameters are inadequate for intrauterine insemination (IUI) or conventional in vitro fertilization (IVF) (1). Although ICSI is increasingly used for the treatment of both male-factor and non–male-factor infertility, the American Society for Reproductive Medicine (ASRM) maintains that there is insufficient evidence to support ICSI use in the presence of normal semen parameters (1). In an earlier study, we found no benefit of using ICSI compared with conventional IVF in

Received September 20, 2017; revised December 15, 2017; accepted December 21, 2017.
A.C.D. has nothing to disclose. A.M. is supported by a research grant from the American Society for Reproductive Medicine. D.M.K. has nothing to disclose. A.K.N. has nothing to disclose. L.W. has nothing to disclose. S.L.B. has nothing to disclose.
The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
Reprint requests: Ada C. Dieke, Dr.P.H., M.P.H., Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, 4770 Buford Highway NE, MS F-74, Atlanta, GA 30341 (E-mail: vts5@cdc.gov).

Fertility and Sterility® Vol. ■, No. ■, ■ 2018 0015-0282/$36.00

https://doi.org/10.1016/j.fertnstert.2017.12.027

the absence of male-factor infertility (2). ICSI use can also be associated with increased health risks for the offspring, including the transfer of chromosomal abnormalities from parent to infant (3, 4), autism (5), intellectual disabilities (6), and birth defects (4, 7), compared with conventional IVF alone.

IVF treatment is costly, averaging $12,400 per IVF cycle, with an additional cost of $1,500 if ICSI is used (8). Out-of-pocket costs associated with IVF treatments have long been considered to be a barrier to care for infertile couples; insurance coverage may provide some financial relief to affected couples, but it is limited. In the United States, 15 states have enacted mandates for private insurance coverage of some type of infertility treatment (e.g., IUI, medications, diagnostic procedures, etc.); 8 states specifically mandate insurance coverage for IVF treatment (Supplemental Table 1): Arkansas, Connecticut, Hawaii, Illinois, Massachusetts, Maryland, New Jersey, and Rhode Island (9). Only 4 of these 8 states explicitly mention ICSI (IL, MA, NJ, and RI). Previously, Jain and Gupta used aggregate IVF data to examine ICSI use in the United States by state mandate status from 1995 to 2004 and found that insurance coverage mandate status was associated with increased ICSI use "not attributed to male-factor conditions" (10). They postulated that ICSI use may be influenced by the presence of mandates requiring insurance reimbursements for IVF services. Because ICSI adds to the overall infertility treatment cost, unnecessary ICSI use may lead to unnecessary financial costs to patients and payers. In recent years, ICSI use for couples without male-factor infertility has been questioned (11) owing to a lack of evidence demonstrating improved fertilization with ICSI compared with conventional IVF. Furthermore, there is some concern that infertility clinics may recommend ICSI even without proper diagnostic workup of the underlying male infertility (12).

Insurance mandates for infertility treatment have been linked to improved ART practices, such as reductions in the number of embryos transferred (13). However, the association between mandates and use of ICSI has not been well described, particularly in recent years. Considering changes in practice, including increased use of ICSI over the past decade, the goal of the present study was to investigate the association between ICSI use and residency in a state with an insurance mandate for IVF treatment.

MATERIALS AND METHODS

This population-based cross-sectional study used data from the National ART Surveillance System (NASS), a web-based reporting system that allows the Centers for Disease Control and Prevention (CDC) to monitor the safety and effectiveness of ART procedures conducted in the U.S. and its territories (14). NASS was established in response to the Fertility Clinic Success Rate and Certification Act of 1992, which requires that U.S. fertility clinics report annual data on ART procedures and outcomes to the CDC. NASS data contains cycle-level information pertaining to patient demographics, reproductive history, ART procedure type, and pregnancy outcomes. NASS also contains information about male-factor infertility diagnosis, but it has very limited details on semen parameters or the severity of male-factor infertility for the years included in the present study.

This analysis focused on fresh-embryo cycles performed during 2000–2015. Because information on ICSI procedures is not consistently collected for frozen-embryo transfers, frozen cycles were excluded. Additional exclusion criteria included: IVF cycles that were cancelled before egg retrieval; cycles from U.S. territories, non-U.S. residents, and gestational carriers; gamete intrafallopian transfer; and zygote intrafallopian transfer cycles. States were classified into two groups: those with an explicit infertility insurance mandate to cover IVF (n = 8; AR, CT, HI, IL, MA, M.D., NJ, and RI) and those without such mandates (n = 43; the remaining 42 states and DC). Because ICSI is performed with IVF, we assumed that the bulk of the ICSI procedure cost would be covered by the IVF mandate. In addition, we performed a sensitivity analysis of just those states that specifically mention ICSI in their coverage details. States were classified as having a mandate only in the years that a mandate was present; because NJ and CT mandates were enacted during the observation period, in 2001 and 2005, respectively, these states were classified as mandate states only for the years following the legislation (2002–2015 and 2006–2015, respectively).

To assess differences in linear trends in ICSI use by mandate status over the study period, we used linear regression models, with ICSI use as the dependent variable and year of cycle start, mandate status, and the interaction of these terms included as independent variables. We restricted the study population to the most recent 5-year period (2011–2015) and used chi-square tests to compare the distribution of patient and treatment characteristics for cycles in states with and without a mandate. We considered the following variables for each patient: age, race/ethnicity, infertility diagnosis, number of previous live births, number of previous spontaneous abortions, number of previous ART cycles, oocyte/embryo source, number of oocytes retrieved, number of embryos transferred, embryo stage at transfer (days 2–3 or days 5–6), number of embryos cryopreserved, use of assisted hatching, and preimplantation genetic testing. We also compared ICSI use for selected non–male-factor indications by mandate status, including: use of preimplantation genetic diagnosis (PGD)/preimplantation genetic screening (PGS), maternal age $\geq$38 years, low oocyte yield (<5 oocytes retrieved), unexplained infertility, and having had two or more previous ART cycles and no history of live births (proxy for previous unsuccessful cycles). Data were missing for <2% of patient and treatment characteristics except race/ethnicity (35.0%) and variables not collected for cycles cancelled between oocyte retrieval and embryo transfer (number of embryos transferred, embryo stage, and use of assisted hatching).

We also used log binomial regression to calculate adjusted risk ratios (aRRs) for the association between ICSI use and mandate status for 2011–2015. Generalized estimating equations (GEEs) were used to account for correlation of outcomes from the same clinic. The variables used in the multivariable analysis were based on a priori knowledge of potential confounders (15). We controlled for female patient