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INCREASING TREND OF IN VITRO FERTILISATION

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Abstract

The advances in the world of IVF during the last decades have been rapid and impressive and culture media play a major role in this success. Until the 1980s fertility centers made their media in house. Nowadays, there are numerous commercially available culture media that contain various components including nutrients, vitamins and growth factors. This review goes through the past, present and future of IVF culture media and explores their composition and quality assessment.

Keywords: *IVF, Quality, Assessment*

INTRODUCTION

The great improvement in culture conditions and especially IVF culture media is an important part of this success. The commercialization of culture media has created competition, has increased the standards and has brought into clinical practice a variety of options. In contrast to media produced in house, there are now strict manufacturing and quality assessment requirements, improved batch-to-batch consistency and less contamination .

In metro cities like Delhi, Mumbai, and Chennai, over 15% of the male population is infertile, a rate greater than that of the female. Stress, obesity, sedentary lifestyle, smoking and alcohol consumption increases the chances for the sperms to die. The changing lifestyle and the polluted environment is one of the main contributing factors to cause infertility in male and increases the chances of miscarriage.

There are a lot of heavy metals, which directly affects the hormones in the body. Reduction in androgens like testosterone in male and estrogen level in female results in loss of libido. A higher concentration of free radicals in the blood causes a lower sperm quality in men.

With increasing age, the sperm motility and the quality decrease causing fertility issues and loss of libido in men.

Thus, owing to the above said reasons, there is increase in the cases of male and female infertility and thus an increasing trend of IVF. IVF is a great treatment method which helps these patients to fulfill their desire of parenthood. The need of the hour is to understand the importance of a healthy lifestyle to increase and maintain fertility.

The introduction of intracytoplasmic sperm injection (ICSI) in 1992 revolutionized the treatment of couples with male factor infertility and made paternity possible for a large proportion of men with non obstructive azoospermia, or no measurable sperm count.[1,2] Over the past 2 decades, the use of ICSI for patients with borderline or even normal semen characteristics has increased,[3] without clear evidence of a benefit to using ICSI over conventional in vitro fertilization (IVF).[4-6] The Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology concluded that there is insufficient evidence to support the routine use of ICSI in patients without male factor infertility.[7] Although ICSI may have a role in IVF cycles using preimplantation genetic testing, in vitro maturation, or previously cryopreserved oocytes, the routine use of ICSI for these indications requires further investigation.[7]

In contrast to conventional IVF, ICSI bypasses natural barriers to fertilization, thereby increasing the possibility of the transmission of genetic defects from one generation to the next. Pregnancies resulting from the use of ICSI have been associated with 1.5 to 4 times increased incidences of chromosomal abnormalities,[8,9] imprinting disorders,[10] autism,[11] intellectual disabilities,[11] and birth defects[12,13]compared with pregnancies resulting from conventional IVF. These increased risks may be related to the effects of underlying male or female sub-fertility, other medical factors present in couples who are candidates for ICSI, or the ICSI procedure.

Intracytoplasmic sperm injection is also considerably more expensive than conventional IVF and adds to financial burdens already experienced by many couples undergoing fertility treatment.[14,15] The higher reimbursement associated with ICSI has been postulated as one possible reason for the increasing use of this technology.

The aim of this study was to assess national trends and reproductive outcomes of fresh IVF cycles associated with the use of ICSI compared with conventional IVF with respect to clinical indications for ICSI use.

All data used in this study were derived from the National Assisted Reproductive Technology Surveillance System (NASS), a data reporting system for the federally mandated collection of information on all assisted reproductive technology (ART) cycles performed in the United States.[16] In NASS, ART cycles are defined as fertility treatments in which eggs and sperm or embryos are handled (manipulated) for the purpose of establishing a pregnancy. NASS includes cycle-level information on patient characteristics, clinical characteristics of the ART

procedure, and pregnancy outcomes. Multiple cycles among individual patients are not linked. NASS captures information from an estimated 97% of ART cycles performed annually.

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Each year, 7% to 10% of reporting clinics are randomly selected for validation and their reported data are compared with medical records. Discrepancy rates are calculated and are less than 5% with the exception of the following infertility diagnoses: diminished ovarian reserve (8.4%), other factor (9.5%), and unknown factor (6.5%).[17]

Because information on ICSI use is not consistently collected across clinics for frozen embryo cycles or cycles canceled prior to oocyte retrieval (ovarian stimulation or monitoring was initiated but cycle did not proceed to oocyte retrieval), we restricted our analysis to all fresh (embryos transferred without being frozen) conventional IVF and ICSI cycles performed from 1996 through 2012 in which oocyte retrieval was attempted. We used linear regression models to assess trends in the use of ICSI for all fresh cycles and for those with the following indications: male factor infertility (infertility due to abnormal semen characteristics, abnormal sperm function, or surgical sterilization), unexplained infertility (infertility with unidentified etiology), female patient aged 38 years or older, 2 or more prior ART cycles and no prior live birth, low oocyte yield (<5 oocytes retrieved), and use of preimplantation genetic testing. Annual ICSI rate was the dependent variable and year was the continuous predictor. Data collection for preimplantation genetic testing was implemented in 2004; thus, we evaluated this factor only for 2004 through 2012.

To account for advances in ICSI techniques and technology, we subsequently restricted the analysis to the 5 most recent years (2008-2012) and evaluated the association between ICSI and reproductive outcomes. We compared the distribution of patient and clinical characteristics between cycles using conventional IVF and ICSI, stratified by male factor and non– male factor infertility. The characteristics assessed in this study included female patient age, race/ethnicity (as reported by clinics), infertility diagnosis, number of prior live births, number of prior spontaneous abortions, number of prior ART cycles (includes prior fresh and frozen cycles), use of donor egg or embryo, use of donor sperm (including cycles using only donor sperm or mixed patient and donor sperm), number of oocytes retrieved, number of embryos transferred, embryo stage at transfer, number of embryos cryopreserved, use of assisted hatching (the purposeful disruption of an embryo's zonapellucida by laser,

mechanical, or chemical means), and use of genetic testing. Race/ethnicity was assessed for reported variations in IVF birth outcomes. NASS does not collect information on fertilization rates; therefore, we indirectly assessed rates of failed fertilization by calculating the percentage of cycles cancelled between retrieval and transfer for cycles using conventional IVF or ICSI, stratified by male factor and non–male factor infertility. We also compared rates of implantation, clinical intrauterine pregnancy, live birth, miscarriage, multiple live birth, preterm delivery (<37 weeks' gestation), and low birth weight (<2500 g) for each strata.

To account for potential confounding by factors associated with ICSI use, we estimated propensity scores using logistic regression models with ICSI as the outcome and included all baseline covariates that may predict probability of treatment selection (age, infertility diagnosis, number of prior live births, number of prior spontaneous abortions, number of prior ART cycles, use of donor egg or embryo, use of donor sperm, and number of oocytes retrieved). Backward selection with a significance level of $P<.05$ was used to determine the final models. Separate propensity score models were estimated for cycles with and without male infertility. Because covariate adjustment using propensity scores produces unbiased estimates of rate ratios, we included the estimated propensity scores in all outcome models.

DISCUSSION

We used robust Poisson regression models with generalized estimating equations for clustering by clinic to estimate unadjusted and adjusted risk ratios for the association between the use of ICSI and reproductive outcomes. The multivariable models included the aforementioned patient and clinical characteristics except race/ ethnicity because of a high percentage (39.7%) of missing information. The models for cycle cancellation did not include assisted hatching, number of embryos transferred, and embryo stage at transfer because this information is not available for canceled cycles. Data were missing for less than 2% of all other covariates.

We also compared reproductive outcomes for conventional IVF and ICSI for subgroups with selected indications including unexplained infertility, age 38 years or older, 2 or more prior ART cycles and no prior live birth, low oocyte yield, and use of genetic testing. All models included propensity scores derived from indication-specific logistic regression models using backward selection with a significance level of $P<.05$.

For bivariable comparisons, we used Pearson χ^2 tests and applied the Bonferroni method to control the familywise error rate due to multiple comparisons. We considered each stratum a

"family" and multiplied the *P* values by 20. For the multivariate models, we also used the Bonferroni method to adjust the *P* values for the 8 outcomes assessed within each indication. A2-tailed *P*<.05 was considered statistically significant. SAS version 9.3 was used for all analyses. The study was approved by the Centers for Disease Control and Prevention's institutional review board. A waiver of informed consent was obtained.

We found that ICSI use increased in the absence of any indication,thereby suggesting that the decision to perform ICSI instead of conventional IVF was likely being influenced by other unmeasured factors. The Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology statement that the use of ICSI for unexplained infertility, low oocyte yield, and advanced maternal age did not improve clinical outcomes was released only recently, in 2012[7]; it remains to be seen how this statement might affect the use of ICSI for non–male factor indications in the future.

Our results demonstrated no improvement in postfertilization reproductive outcomes with use of ICSI over conventional IVF in the absence of male factor infertility, regardless of the underlying indication for use. On the contrary, reproductive outcomes were slightly poorer when ICSI was used in non–male factor cases.

CONCLUSION

We found that use of ICSI was associated with lower rates of multiple birth regardless of whether male factor infertility was present; however, this finding may be due to lower implantation rates in cycles where ICSI was used. Our findings were consistent with those of a previous randomized clinical trial, which found only marginal increases in implantation and pregnancy rates in couples undergoing conventional IVF compared with ICSI in the absence of male factor infertility, leading the authors to conclude that ICSI offered no clinical advantage over conventional IVF in cases of non–male factor infertility.

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