



Optimizing Reproductive Autonomy in Cystic Fibrosis: The Role of Oocyte Cryopreservation

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Cystic fibrosis (CF), an inherited genetic disorder compromising the body's viscera, is a major contributor to infertility in women of reproductive age. Because of dysfunctional activity of cystic fibrosis transmembrane conductance regulator (CFTR), women with CF may have thicker cervical mucus. A thicker mucus can prolong the time to get pregnant by making it more difficult for sperm to pass through the cervix. Delayed conception or female infertility may result from changes in uterine pH balance, protracted puberty, and irregular menstruation (1). The establishment of patient registries, CF care centers, as well as the implementation of early diagnostic and screening programs have culminated in substantial advancements in CF prognosis, with life expectancy now extending into the late 40s and 50s. Oocyte cryopreservation (OC), particularly through vitrification, can substantially enhance the fertilization and later productive outcomes in either surrogacy or assisted reproduction. Oocyte cryopreservation may provide a suitable alternative to increase fertility by 34-35%. However, it remains a largely neglected technique in CF, despite its widespread use in oncology, mainly due to technical challenges associated with the mature ovum including its large size, low surface area to volume ratio, and limited cell number (2). The success rates have reached unprecedented levels by using ultra-rapid vitrification techniques and intracytoplasmic sperm injection (ICSI). Advances such as artificial intelligence-based image analysis and spindle visualization using polscope technology are expected to further enhance the accuracy and reliability of this technique. In women

with CF, more than 50% can conceive without the use of assisted reproductive approaches, although the overall fertility remains reduced (3). Compared to women of similar age, estimates of subfertility and infertility are higher among those with CF. This issue is exacerbated by factors such as the presence of thickened cervical mucus, which can impede sperm motility and alter the bicarbonate (HCO₃) and pH balance in the uterus, therefore affecting sperm capacitation. Some women with CF may experience irregular menstruation, delayed puberty, or amenorrhea, all of which can significantly impair normal ovulation and fertility. Moreover, women with CF may also experience cystic fibrosis-related diabetes (CFRD) and inflammation, which can also play an important role in decreased ovarian reserves due to low anti-Müllerian hormone (AMH) levels. A study conducted in 2021 found that the number of ovarian follicles decreases with age, with the rate of decline being steeper in women with CF (3).

Couples affected by CF require comprehensive counseling when planning to start a family. Women with CF require support to make informed, patient-centered reproductive decisions for themselves as they plan for their future family by consulting a doctor or a health professional (4). This can be achieved by educating them about advances in the technique, such as assisted reproductive technology (ART). Although some CF-specific guidelines exist, they are not widely disseminated; these include the use of ovulation-inducing medications, intrauterine sperm insemination, in vitro fertilization (IVF), and cryopreservation techniques. Cryopreservation is a technique used to

freeze biological materials like cells or tissues, although OC is mostly used in fertility treatments.

When using frozen oocytes, there are no significant differences in fertilization or pregnancy rates, and the clinical outcomes are generally favorable (5). OC, which is age-dependent with respect to oocyte quality, is most affected when performed in the early stages of reproductive life, ideally in the early to mid-20s. According to the study in 2024, among women who underwent planned OC, those aged 40 and older had lower birth rate compared to the women under 35, with an overall oocyte survival rate of 78.5%. The whole method is highly safe and effective as a result of advancements made in cryotechnology and research on oocyte structure and integrity. In another study, 748 oocytes were cryopreserved, with a survival rate of 76.1%, a fertilization rate of 66.2%, and 39.1% reaching the blastocyst stage (6). Planned OC provides social revolution and reproductive autonomy for women, particularly prior to lung transplantation or long-term therapies that compromise fertility, thereby increasing the potential for successful reproduction.

With the progress in CF care, it continues to improve the life expectancy of women living with CF; hence, their reproductive futures must not be overlooked. OC represents a feasible alternative in fertility preservation, and opportunities for child-bearing are increasing in a healthier context (6). Integrating personalized conception planning with early OC is a primary consideration in reproductive care counseling and routine assessment of oocyte reserve, aimed at safeguarding reproductive autonomy, and optimizing the likelihood of healthy live births in women with OC. Multidisciplinary collaboration is crucial, as each specialist contributes to the effectiveness of patient care. For instance, genetic counselors provide guidance on the hereditary nature of CF, while reproductive

endocrinologists analyze ovarian reserve and overall reproductive potential. Given the reproductive challenges faced by women with CF, there is an urgent need for CF-specific reproductive guidance, including information on fertility preservation options such as OC, the impact of CFTR modulators, and the use of medications to address these complications (7). Addressing the aforementioned barriers is essential to uphold reproductive autonomy and enable women with CF to overcome fertility limitations.

Conflict of Interest

Authors declare no conflict of interest.

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