

Fears surrounding pregnancy and motherhood among women with cystic fibrosis

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Recent advances in science and clinical care have changed the characteristics of the population with cystic fibrosis (CF). Half of patients with CF are now adults who want to achieve milestones that were impossible in the past; for women with CF, this may include motherhood. However, these women may have concerns and fears about getting pregnant, being pregnant, and becoming mothers that go beyond those that otherwise healthy women experience. This qualitative study was conducted to ascertain the reproductive health concerns of a small group of women with CF.

KEY WORDS: cystic fibrosis, pregnancy, motherhood, fertility, reproductive health, qualitative study

Cystic fibrosis (CF) is an autosomal-recessive, multisystem disease affecting about 70,000 persons worldwide.¹ In the United States, 1 in 31 persons of Caucasian European descent carries the CF trait, making it the most common genetic disorder in this group.¹ A defect on chromosome 7 results in an alteration in the structure and function of the CF transmembrane conductance regulator (CFTR) protein that controls movement of ions across cell membranes.² As a result of the impaired CFTR protein, the body produces tenacious mucus that obstructs certain organs, particularly the lungs, intestines, and those of the reproductive tract.²

Recent advances have improved overall survival and quality of life (QOL) of patients with CF. For the first time since the CF gene was identified in 1989, about half of patients with the disease survive to adulthood.¹ Average life expectancy has risen from 14 years in 1969 to 40+ years today.^{1,3} Women, who account for about half of the CF population,⁴ experience poorer health-related QOL than their male counterparts.⁵ In women with CF, hormonal fluctuations across the lifespan may compromise their overall health.⁶ Nevertheless, many women with CF wish to experience all of the adult developmental milestones that may not have been

One fear before pregnancy was bearing a child with cystic fibrosis.



possible in the past, when CF was considered a life-limiting disease of childhood.⁷ One of these milestones is becoming a mother.

The wide variability in disease presentation means that some women with CF can conceive a child naturally and easily, whereas others have impaired fertility or infertility. Thickened cervical mucus can obstruct the Fallopian tubes and/or the cervix, preventing sperm from reaching the egg for fertilization.¹ The thickened mucus in the gastrointestinal tract impedes proper absorption of nutrients.¹ Adequate body fat and weight are needed for a regular menstrual cycle; as a result, some women with CF who have a suboptimal body mass index (BMI) have irregular ovulation.¹ In general, good pulmonary function and a normal BMI predict reproductive success in women with CF.⁸

Great strides have been made since 1960, when it was reported that a successful pregnancy in a woman with CF ended with maternal death from CF complications 6 weeks after delivery.⁹ Although exact fertility data are unknown, the CF Foundation Patient Registry indicated that the number of women with CF who became pregnant more than doubled in 24 years, from 116 in 1992 to 270 in 2016.⁴ With recent CF drug discoveries that target specific CF mutations, the personalized approach to care will likely lead to improved patient outcomes, including the ability to become pregnant

and deliver healthy infants.

Despite these promising developments, Korzeniewska et al¹⁰ reported that only 33% of their sample of women with CF (n = 64) understood how CF affects fertility. Based on semi-structured interviews with 22 women aged 18-30 years with CF, Kazmerski et al¹¹ found that misinformation regarding how CF could affect fertility and pregnancy abounded. In a separate report, Kazmerski et al¹² indicated that the women with CF were disappointed by the lack of support from their CF care team when the topic of reproductive health was raised, usually by patients themselves. Both patients and care team members agreed that improvements in this area were needed.

The purpose of the current study was to ascertain the reproductive health concerns of a group of women with CF. These women were part of a larger mixed-methods study (the parent study) that investigated their knowledge of basic fertility concepts and how CF affects the reproductive system, and explored their perceptions regarding whether new CFTR-modulating drugs could affect their reproductive health.⁷

Parent study

The parent study evaluated broad reproductive health implications of targeted therapy for young women with CF.⁷ It was approved by the University of Alabama at Birmingham Institutional Review Board and conducted in Alabama in 2015-2016.

In brief, 10 women aged 25-34 years with a confirmed diagnosis of CF homozygous F508del mutation and a forced expiratory volume in 1 second $\geq 40\%$ participated.⁷ They were recruited from an adult CF center located in a large academic medical center in the southeastern United States.

Participants completed a demographic survey and two questionnaires related to their knowledge of fertility and CF and sat for an audio-recorded, semi-structured interview about the processes of becoming pregnant and a mother. Individual interviews lasting 30-45 minutes were conducted in person or by telephone by two of the authors, who also completed the qualitative analysis for the current study. Participants were asked whether they had been pregnant, whether they felt that CF affected their fertility, how and when they learned that CF might affect fertility, what they knew about the effects of the CFTR-modulating drug lumacaftor/ivacaftor (LUM/IVA) on fertility, and whether they knew about available resources on pregnancy and fertility. Thematic saturation was reached after the eighth interview. Findings from the parent study showed that participants reported needing comprehensive reproductive and sexual health counseling and education from their CF care team, as well as support for their desire to become mothers even though they suspected that their fertility might be impaired.

Current study

Among the 10 women, 7 elaborated on their concerns and possible challenges to becoming pregnant, with 2 also describing their experiences with past or current pregnancies. Qualitative data were analyzed using Braun and Clarke's approach to thematic analysis, which included these steps: (1) Interview transcripts were read multiple times to look for patterns; (2) Data about fears related to pregnancy and motherhood were coded with descriptive labels; (3) Codes were grouped into preliminary themes; and (4) The final thematic schema was identified.¹³ Two authors independently reviewed all transcripts and coded the data, and collaborated in developing the final coding schema. Both authors had >90% inter-rater agreement during the coding phase and easily arrived at consensus during the thematic development phase. HyperRESEARCH, a qualitative analysis software, was used to manage and analyze the data.¹⁴

Findings

Participants (mean age, 29 years) were Caucasian and highly educated, with 80% having a 4-year college degree. Most were married and had never been pregnant. They hoped that new targeted therapeutics in CF care would help them conceive and carry a healthy pregnancy to term. They expressed different layers of fears as they contemplated their future on the pregnancy continuum. (Pseudonyms are used to protect their identities.) The main theme that emerged from this qualitative analysis was **Fears surrounding pregnancy and motherhood**. Although most participants said they desired children, they had fears related to getting pregnant, being pregnant, and becoming new mothers—the three subthemes.

Fears before pregnancy

Five participants reported having fears even before attempting pregnancy. One fear was bearing a child with CF. Carly said that it was critical to have her partner tested for the CF gene prior to exploring her options for motherhood because she did not want to risk having a child with CF: *We decided [that] if he was a CF carrier, we would adopt. If he was not a CF carrier, we would try [to get pregnant]. Being a mother with a child with CF, it just scared the living crap out of me.* Experiencing the daily struggles and treatment burden of CF, Carly did not want the same hardships for her child. Debby echoed the sentiment about her partner carrying the CF gene: *We are interested in confirming that he's not a carrier because if he is a carrier, we know our chance of having a CF baby would be definitely increased. If that is the case, we would want to look at alternative situations, like adoption.*

Two participants described financial concerns related to becoming pregnant. Ella said that if she could not get pregnant, she wanted to explore using a gestational carrier. However, she stated: *I just don't think we can afford surrogacy.* Anna, who has a school-age child, feared having another child: *My fears would be financial concerns, just making sure I can cover all the bases so that my next pregnancy is as smooth, or as close to as smooth, as the first one.*

Gia shared concerns related to LUM/IVA, a part of her regimen that benefited her overall health and functioning. Because LUM/IVA's safety during pregnancy has not been established, Gia feared that she would need to stop her medication if she were to become pregnant. She stated: *My biggest concern is how I would feel going off lumacaftor/ivacaftor. [I would] take a hit to my health, my lung health, [and worry] if*

that is going to impact the health of a fetus....and [if] somehow I wasn't able to carry the baby to term.

Fears during pregnancy

Five participants conveyed fears about the pregnancy itself. Most fears centered on keeping themselves as healthy as possible in order to deliver a healthy baby. Betty and Carly described how maintaining their health during pregnancy and afterward was critical in order to care for their infants. Carly, a natural athlete who enjoyed exercise as part of her health regimen, said: *My biggest fear with having CF is how uncomfortable [pregnancy] is, and I worry that my athleticism, working out, is gonna have to decrease....that [it] may lead to lower lung function. That scares me. I don't care about what I look like on the outside for the most part; I care about the lungs.*

Ella feared that a pregnancy could compromise her pulmonary status: *I worry about [pregnancy] impacting my lung function in a way that could be permanent. When lung function goes down, there could be scarring, and things that occur that make it irreversible.* Fran worried about her pulmonary health but had a more positive outlook on pregnancy's potential effects: *I think I'm strong enough to handle it. If I did lose lung function, I would be dedicated to getting it back. That would be a top priority for me. It [having a baby] would be worth a short-term setback.* Debbie described how she was proactive about maintaining her treatment regimen and staying healthy to avoid getting sick and harming the baby.

Fears as new mothers

Six participants reported potential fears as new mothers, most of which related to balancing the demands of CF with work, family, and motherhood. Ella reported: *I do worry about*

being able to balance doing all of my treatments and caring for a newborn. Debbie described her fear of being able to care for both herself and a baby: *I wanna make sure that I'm able to take care of the baby as well as myself.* Gia expressed her worry about being able to balance her job and CF with being a mom: *I guess it's more of the balance of, "Could I keep working and how much?" and maybe needing to downshift. I sometimes worry about CF, [which] is already such a time suck that it's like, "Oh, let's throw a baby into the mix and see what happens."*

Two participants expressed worry about their child going to daycare and bringing home contagious infections. Carly said that she was always vigilant about possible infection sources to keep herself healthy: *I'm a total germophobe. My biggest fears are just me getting sick and not being able to take care of my baby, because of whatever bugs [he or she] might have.* She went on to discuss not being able to be around or care for her baby when he or she got sick: *I'm gonna have to quarantine myself into a room... [and not] get sick so I can take care of my baby.* Betty discussed getting sick from her baby as a result of going to daycare: *They [babies] go there and they get sick. They come back, I get sick.*

In thinking about their futures, two participants mentioned the often unspoken fear of dying early of their incurable disease and not being able to be there for their children. Ella said: *I think about not being healthy, or putting my child through the trauma of losing a parent. I think about how wonderful my husband is, and my family. If that [death] were to happen, it wouldn't be as though [my baby] would be left alone in the world.* Anna spoke of the fear of dying in a more positive light, as a source of motivation: *Yeah, dying early. That's a big fear. That also keeps me mo-*

tivated. Other participants voiced the positive aspects of becoming pregnant and being mothers with CF. Anna, who had CF-related diabetes, stated: *My A1Cs stayed in the 6's during my entire pregnancy—the best they've been in my life.* Carly reflected on her determination to remain healthy despite the daily challenges of having CF: *I don't feel that CF has held me back in any other aspect of my life. I'm certainly not expecting it to here [pregnancy].*

Discussion

These study participants wanted to experience pregnancy and motherhood, but they had certain fears about these life experiences. Even before contemplating becoming pregnant, some expressed concerns about the genetic transmission of CF. They did not want any children they bore to experience a life-limiting disease. They wanted their partners to be tested for CF to rule out the possibility of having a child with CF and to help inform their decision-making with regard to the use of gestational carriers, adoption, or living a child-free life.

Concerns about genetic transmission of CF are understandable; young women with breast cancer who carry the *BRCA* gene have expressed similar fears. In response, the American Society of Reproductive Medicine has recommended pre-implantation genetic diagnosis (PGD) testing on embryos to look for a specific genetic disorder such as the *BRCA* mutation.¹⁵ In fact, CF is one of the most common indications for PGD testing, enabling couples to transfer an embryo without the CF gene and avoid the difficult decision to terminate a pregnancy.¹⁶

The physical stress of pregnancy, combined with potential adverse effects of a medication regimen (or temporarily stopping such a regi-

men), is challenging for women with a chronic illness such as cancer or diabetes or a history of childhood cancer. They have concerns about potential health setbacks such as a recurrence or the development of secondary cancers or pregnancy-associated cardiomyopathy.¹⁷⁻²¹ Despite having similar fears, the women with CF in this study expressed hope and determination to experience pregnancy and motherhood.

Many survivors of childhood cancer who are at risk for infertility related to gonadotoxic therapy have misperceptions regarding their personal risk for infertility.²²⁻²⁶ The American Society of Clinical Oncology recommends discussing potential infertility, as well as fertility preservation options, with all young individuals diagnosed with cancer.²⁷ Multidisciplinary programs to address fertility preservation in children and adolescents are emerging.²⁸ The Cystic Fibrosis Foundation aims to provide resources to educate patients, families, and healthcare providers (HCPs) regarding fertility and reproductive health options.²⁹

A sobering challenge of future motherhood for women with CF is the potential for early mortality, which forces them to face an uncertain future for themselves as parents and for their children, who could suffer the loss of their mother at a young age. Confronting these uncertainties appeared to strengthen the resolve of some of the study participants with CF, and could potentially motivate them to remain engaged in health-promoting activities and to maintain strong relationships with their partners and family members.

Limitations

A limitation of the current study was the small and homogenous (all Caucasian) sample, although this demographic characteristic is

Attempting and carrying a pregnancy is a complex challenge for women with CF.



representative of the CF population. Another limitation is that these women had the same genetic mutation (F508del homozygous), which may have influenced their responses because of the moderate/severe phenotypic presentation of this mutation. Finally, 80% of the participants held a 4-year college degree, compared with 30% of persons with CF nationally, which could limit the generalizability of the findings.⁴

Implications for practice and future research

Childbearing-age women with CF may benefit from a collaborative care effort between the CF care team and reproductive health specialists who can provide individualized education and counseling. All of these HCPs can address patients' fears and assist them with their reproductive health decisions. Kazmerski et al¹² reported that women with CF considered their disease a major factor in deciding whether to become pregnant, and that they were disappointed by the lack of support from their CF care team when the topic of reproductive health was raised, usually by the women themselves. HCP and patient discomfort in initiating reproductive and sexual health discussions may hinder provision of comprehensive care; hence, HCP training and educational resources for reproductive health services, as well as standardization in CF care

models, are warranted.¹¹

Additional research is needed to investigate how women with CF decide to pursue a pregnancy versus use a gestational carrier or adopt a child. The different paths to motherhood for women with CF is not well documented; in fact, in the larger (parent) study, these women self-reported a lack of knowledge related to alternative options and their associated costs, both tangible and intangible.⁷ These findings are consistent with those of Cherven et al,²⁶ who found that only 36% of childhood cancer survivors reported receiving education about the risk for infertility at diagnosis and 39% received it at the end of therapy. Nearly all of these survivors reported that they would have preferred receiving fertility education at diagnosis. However, education at one time point alone may be insufficient. Continuing discussions about fertility need to be targeted to young cancer survivors' needs and developmental stage, which change over time. Findings from previous work with young cancer survivors may help improve the conversation with patients with CF, who require ongoing education and counseling about reproductive health and fertility options, as well as their associated costs.

Conclusion

Attempting and carrying a pregnancy is a complex challenge for women with CF. If these women can conceive,

then they worry about being able to be a full partner in caring for a newborn—while still sustaining their own daily care for CF. As mean survival of patients with CF extends into the fifth decade of life, findings from this current study suggest that women with CF would benefit from individualized education and counseling regarding reproductive health as part of their comprehensive clinical care. ●

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