

# ADVANCED CLINICAL PHARMACOLOGY AND TOXICOLOGY, THERAPEUTICS

## Cystic Fibrosis and Pregnancy

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#### **INTRODUCTION**

Cystic fibrosis (CF) is a genetic disorder that affects mostly the lungs, but also the pancreas, liver, kidneys, and intestine. Long-term issues include difficulty breathing and coughing up mucus as a result of frequent lung infections. Other signs and symptoms may include sinus infections, poor growth, fatty stool, clubbing of the fingers and toes, and infertility in most males. Different people may have different degrees of symptoms.

+ Other complications of cystic fibrosis include pancreatic insufficiency, diabetes, osteoporosis, liver disease and gallstones. There are approximately 8000 people living with cystic fibrosis in the UK and 1 in 25 of the population is a carrier of the cystic fibrosis gene mutation. The outlook has improved dramatically because of improved diagnosis and management median survival in the UK is now 31 years.

Recent studies have shown, however, that sexual adaptation is normal and that sexual activity is not delayed when compared with adolescents without cystic fibrosis. + Menstruation generally occurs slightly later in girls with cystic fibrosis and bodyweight is the most significant determinant of menarche. Once menstruation is established, the majority have regular cycles, with amenorrhea most likely to occur in girls with poor lung function. Nearly all men with cystic fibrosis are infertile but women with cystic fibrosis have relatively normal fertility, despite having thickened cervical mucus which does not show the usual cyclical variation.

+ Contraception is important for those wishing to avoid pregnancy and this needs to be discussed early, as unplanned pregnancy can be disastrous. Choice of contraceptive method can be difficult because of potential interactions with cystic fibrosis and its treatment but the risks of contraception need to be balanced against the risk of unplanned pregnancy. The Combined Oral Contraceptive pill (COC) is the most frequently used method. There are concerns that it could be less effective in women with cystic fibrosis, in view of the frequent courses of antibiotics required; however, there have been no pregnancies reported as a result of COC failure. It is important to advise on the use of additional contraception (For example, condoms) when a woman is taking antibiotics. Long-term methods, such as Depo-Provera®, Implanon® and the Mirena® intrauterine system, are highly effective and avoid concerns regarding malabsorption. Long-term use of Depo-Provera can, however, aggravate osteoporosis, a common complication of cystic fibrosis. If termination of pregnancy is required, the usual methods (Surgical or medical) can be used.

Approximately 30-40 women with cystic fibrosis undertake pregnancy each year in the UK. Early reports suggested that pregnancy was associated with high rates of miscarriage, premature delivery and stillbirth. The proportion of live births is now 70-90% and the spontaneous miscarriage rate is no higher than in the general population.

- + Pre-existing and gestational diabetes are more common in pregnancies in women with cystic fibrosis (incidence 14-20%) and increase the risk of pregnancy complications, including preterm delivery and stillbirth. + The mode of delivery depends on obstetric indications, maternal health and gestational age.
- + Caution regarding pregnancy is advisable, however, as individual women respond differently and some women's health will deteriorate during and after pregnancy. The long-term prognosis needs consideration, as 20% of mothers will not live to see their child's tenth birthday, rising to 40% for those women with poor lung function at the beginning of pregnancy.
- + Women with good pre-pregnancy lung function (FEV1 70% predicted) tolerate pregnancy very well and have the most successful outcomes and lowest maternal mortality.

Women with cystic fibrosis who have undergone lung or heart-lung transplants and who are contemplating pregnancy merit special



consideration. Women are generally advised to wait 2-3 years post-transplant before considering pregnancy to ensure graft stability and to reduce the risk of rejection.

- + A thorough assessment of the severity and rate of progression of the disease is crucial to obtain accurate information about the likely outcome of pregnancy and its effect on maternal health. Frank discussion about the challenges of parenthood when coping with a life-limiting disease is important. The possibility of maternal death and a partner being left alone to bring up a young child is a difficult topic to discuss but it should be considered.
- + Partner testing should be offered to estimate the risk of a child being born with cystic fibrosis. All children will be carriers. If the partner does not carry any of the common gene mutations for cystic fibrosis, the risk of having an affected child is 1:250. If the partner does carry one of these genes, the risk is 1:2. If required, antenatal diagnosis can be performed by chorionic villus biopsy in the first trimester. Alternatively, *in vitro* fertilization with pre- implantation genetic diagnosis is an option.
- + Folic acid supplementation is recommended prior to conception and during the first trimester, to reduce the risk of neural tube defects. A glucose tolerance test should be performed for women whose glycemic status is unknown, to look for evidence of cystic fibrosis-related diabetes or impaired glucose tolerance. Women with diabetes should be referred to a specialist in cystic fibrosis related diabetes before conception: optimization of glycemic control will reduce the risks of congenital malformation and pregnancy complications.
- + A pregnant woman with cystic fibrosis should be cared for by a multidisciplinary team This should include: her cystic fibrosis team (Physician, nurse, physiotherapist and dietician); an obstetrician with experience in cystic fibrosis in pregnancy; a midwife and an obstetric anesthetist.

An individual management plan for delivery should be made, depending on gestational age, disease severity and fetal wellbeing. Elective preterm delivery may be required if maternal health and lung function is declining or if there is evidence of fetal growth restriction. Corticosteroids for fetal lung maturation should be given in these circumstances. Elective preterm delivery is most likely to be by caesarean section. In the majority of cases, if maternal health is well maintained and the fetus is growing normally, vaginal delivery can be anticipated at term. Lung function should be optimized prior to delivery: This may require admission in the third trimester for intensive physiotherapy and antibiotics, followed by induction of labour or caesarean section.

The involvement of anesthetic staff is essential throughout pregnancy and prior to delivery. For caesarean section, regional or general anesthesia can be employed, depending on lung function and infection status. If regional anesthesia is used, an epidural catheter can be left in place to assist with pain relief and postoperative chest physiotherapy. For vaginal delivery, epidural analgesia may be appropriate, to provide pain relief, alleviate maternal fatigue and reduce the risk of needing general anesthesia should emergency caesarean section be required.

Early studies suggested that breast milk in mothers with cystic fibrosis has a high sodium content and that breastfeeding is contraindicated. Subsequent research has confirmed that their breast milk has a normal composition. Breastfeeding is, however, exhausting and uses up calories: women with cystic fibrosis may find it difficult to breastfeed exclusively. If women are unable to maintain their weight, alternative methods of feeding should be discussed. The safety of concomitant maternal drugs should also be taken into account when considering the mode of feeding.

#### **Author Biography**

Having long experience in obstetrics and women health with focus on infertility together with standards of quality in healthcare specially women health. Obstetrics and women health, diploma from Royal college of physicians of Ireland together with 3 practical diplomas in Obstetrics and Gynaecology, infertility and ultrasound and 1st and 2nd part of MRCOG and MRCPI becoming associate of Royal college. In quality of healthcare, American board of quality in health care, fellowship and membership of ISQUA of Ireland together with becoming team steps trainer. In health administration, diploma from Nottingham, Boston and Ain Shams university with minimaster degree from Nottingham in business administration. Now she is working as gynaecologist and obstetrician in maternity hospital, UAE.

#### **Research Interest**

Dr. Weaam Albanna, research interests include understanding of infertility causes, aggravating factors and different methods of treatment together with different topics of women health during pregnancy.

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