Journal of Cystic Fibrosis 13 (2014) 69 – 73

Journal of Cystic Fibrosis

www.elsevier.com/locate/jcf

Original Article

Cystic fibrosis and pregnancy in the modern era: A case control study

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Received 10 May 2013; received in revised form 30 July 2013; accepted 6 August 2013
Available online 7 September 2013

Abstract

Background: Increasingly, women with cystic fibrosis become pregnant. Outcomes of these women need further study particularly in the setting of improved survival in CF.
Methods: We performed a case-control study of pregnant CF women including 22 matched pairs with an average follow-up of 4.5 years. Nutritional outcomes, changes in lung function, and exacerbation rates were compared.
Results: Matched pairs were similar in age, sweat chloride, FEV_1 and FVC % predicted, BMI, and diabetes status. Change in BMI, FEV_1 and FVC % predicted at the end of pregnancy and at last follow-up were similar between groups. Moreover, rates of exacerbation before, during and after pregnancy were similar. On multivariable analysis pregnancy had no effect on change in lung function over the study period. Significant predictors of decline included higher pre-pregnancy lung function and pancreatic insufficiency.
Conclusions: Pregnancy does not lead to immediate or medium-term adverse effects for CF patients.

Keywords: Cystic fibrosis; Pregnancy; Nutrition

1. Introduction

The life expectancy for people with cystic fibrosis (CF) has been steadily rising due in part to improvements in management and expanded treatment options. According to the 2011 Annual Data Report from Cystic Fibrosis Patient Registry, the median predicted age of survival is approaching 40 years [1].

Coincident to improvements in survival, patients are leading healthier and longer lives, and career and family planning is more common for those with CF. As a result, an increasing number of women are becoming pregnant, and recently the 2011 Cystic Fibrosis Patient Registry reported that 211 women with cystic fibrosis became pregnant this past year [1]. Unfortunately, little is known regarding outcomes of cystic fibrosis patients who become pregnant in the most recent era, when compared to peers with similar nutritional and pulmonary status.

Preconception care, including optimizing pulmonary function, improved nutrition and controlling infections more aggressively, favors pregnancy outcomes [2]. Recent studies have confirmed this approach by documenting successful outcomes obtained in pregnant women with CF, with appropriate antepartum, intrapartum and postpartum care [3]. Overall, pregnancy is tolerated well in CF patients with mild disease. In contrast, women with poor pulmonary function, inadequate nutrition, and pulmonary hypertension are at greater risk for maternal and fetal morbidity and mortality. One study found that preterm birth prevalence was as high as 40% in pregnancies of patients with these comorbidities [2]. However, pregnancy in CF patients can lead to little adverse effects in body weight in the post-partum period [4]. Others have documented a decline in post-pregnancy forced expiratory volume in one second (FEV_1) and body mass index (BMI) compared to pre-pregnancy values;

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1569-1993/$ -see front matter
http://dx.doi.org/10.1016/j.jcf.2013.08.004

moreover, increased complications of premature births and low neonate birth weight were noted [5]. Pregnancy has also been associated with increased antibiotic use and number of hospitalizations [6]. FEV_1 below 50% predicted, the presence of *Burkholderia cepacia*, and pancreatic insufficiency have been suggested as predictors of negative outcomes [7]. In summary, these studies suggest that outcomes in pregnant patients with CF need further study, preferably in larger populations and in a more modern era, as new advancements in the field have improved overall survival in CF patients.

We report a matched, case-control study of women with cystic fibrosis who became pregnant and compare their outcomes to women with similar nutritional status, age and lung function but who have never been pregnant. By exploring the outcomes of pregnancy in cystic fibrosis patients, health care professionals can use all the data available to them while educating patients on the risks of pregnancy. The current study is small, but adds further information to the current literature.

2. Methods

This study was approved by the Institutional Review Boards at both Universities affiliated with two adult Cystic Fibrosis Centers in a major metropolitan area (University of Pennsylvania and Drexel University College of Medicine). No personal identifiers were used during the process of data collection.

A two center case-controlled study was performed to examine the outcomes of pregnant cystic fibrosis patients who carried fetuses beyond second trimester (Group A) compared to non-pregnant CF patients (Group B) between 2001 and 2008. Women between 18 and 38 years of age were included.

2.1. Data collection

Demographic and clinical data was extracted from the electronic medical records. Other variables collected included genotype and sweat chloride. Nutritional status (BMI), lung function (FEV_1% predicted), CF-related diabetes, and the number of pulmonary exacerbations were documented during four specific time periods: before pregnancy, end of pregnancy, after pregnancy and at last follow-up (Figs. 2 and 3). *Before pregnancy* was defined as a time period between 1 week and 3 months prior to conception or an estimated time of 10–12 months prior to the delivery date. *End of pregnancy* was defined as early as 2 days up to 3 months of time after delivery. *After pregnancy* was between 3 months up to 12 months after delivery. *Last follow-up* period included results from 12 months up to 5 years after delivery. The average follow-up time was 4.5 years. A timeline graph shown in Fig. 1 defines the time periods indicated by the various groups aforementioned.

In addition, information on microbiology, liver function, vitamin levels and osteoporosis was obtained. Hospitalizations, transplantation or death were documented. Finally, information on education, insurance and marital status was also obtained. Fetal outcomes were tracked, including stillbirths, prematurity, developmental issues and other problems. However, pregnancies that were terminated prior reaching the latter of the 2nd trimester were not documented.

Group A patients were then matched to other female patients who have not become pregnant (Group B) and are followed by the Adult Cystic Fibrosis clinics; first based on age, then based on lung function and finally based on nutritional status. Data described as above was also obtained for the control patients.

2.2. Statistical analysis

Analyses were made by student *t*-test or its non-parametric equivalent to compare the two groups of CF patients. Multivariable linear regression was used to estimate predictors of loss of lung function in the sample of patients. Pregnant patients who could not be individually matched to a non-pregnant patient based on age, FEV_1 and BMI were not included in this study. Also, patients whose information was not available at the end of pregnancy and after pregnancy due loss to follow-up were not included.

3. Results

In the combined Adult Cystic Fibrosis Centers, there are a total of 295 patients in the registry at the end of the study. The median FEV_1% predicted was 65.14 and the median BMI was 22.0 kg/m^2 for the combined cohort from both centers based on the Annual Data Report at the end of the study. A total of 31.5% of female patients in the programs had carried out pregnancies resulting in birth; however, not all pregnancies were included in this case-controlled study as mentioned above. In addition, there was one early termination of pregnancy (first trimester) because of patient preference (patient moderate lung dysfunction, but felt

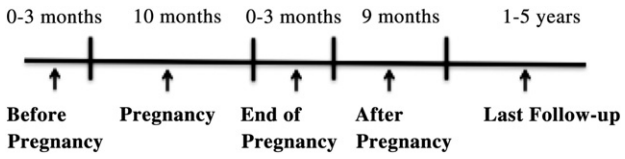

Fig. 1. Timeline graph depicting time period when data was collected in each group (before pregnancy, end of pregnancy, after pregnancy and at last follow-up).

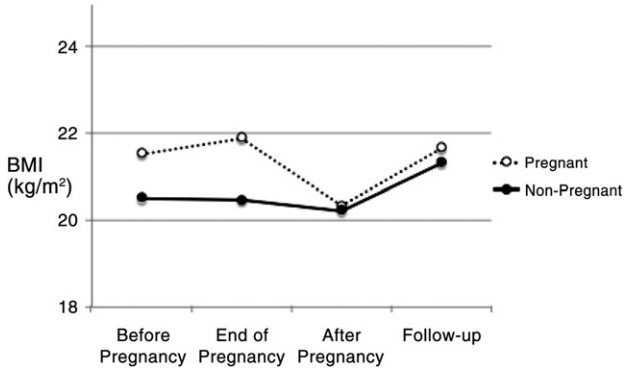

Fig. 2. Average Body Mass Index (BMI) during various time periods in pregnant and non-pregnant cystic fibrosis patients. The follow-up period represents an average of 4.5 years after pregnancy. There is no significant difference in change between BMI at baseline and BMI at the end and after pregnancy ($p > 0.2$).