OBSTETRICS

Pregnancy with Friedreich ataxia: a retrospective review of medical risks and psychosocial implications

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OBJECTIVE: Friedreich ataxia (FRDA) is an autosomal recessive, neurodegenerative disease. Recent medical advances have improved the average life expectancy, and as such, many female patients are contemplating pregnancy. However, little research exists exploring the medical or psychosocial complications that arise from pregnancy with this disease.

STUDY DESIGN: In this study, we retrospectively examined 31 women with FRDA who had 65 pregnancies, resulting in 56 live offspring.

RESULTS: FRDA did not appear to increase the risk of spontaneous abortion, preeclampsia, or preterm birth. Despite the sensory and proprioceptive loss that occurs in FRDA, nearly four fifths of births were vaginal. Of babies, 94.4% were discharged home with their mothers. Equal numbers of women reported that pregnancy made their disease symptoms worse, better, or unchanged.

CONCLUSION: This study demonstrates that women with FRDA can have uncomplicated pregnancies that do not uniformly complicate disease symptomatology.

Key words: autosomal recessive genetic disease, family planning, Friedreich ataxia, neurodegenerative disease, pregnancy with disability

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Friedreich ataxia (FRDA) is a neurodegenerative, autosomal recessive genetic disorder characterized by dysarthria, ataxia, loss of reflexes, scoliosis, cardiomyopathy, and balance difficulties.[1-4] Typical onset occurs in late childhood or early adolescence, but is variable.[3] Of people with FRDA, 97% have an expanded GAA triplet repeat in both alleles of the *FXN* gene, and the length of the shorter GAA repeat correlates with age of onset ($r = 0.6$-7).[5-7] The remaining 3% of patients carry an expanded GAA repeat on one allele, and a point mutation on the other allele.[8-10]

With improved cardiac care, spinal fusion surgery, and other medical interventions, the mean life expectancy of FRDA has likely improved significantly beyond the previously reported age of 37 years.[11] As a result, a significant number of women with FRDA are contemplating pregnancy. Many are seeking specific guidance on family planning, an issue that has not been adequately addressed.

Few studies have examined disease-associated medical risks and/or psychosocial implications of pregnancy in women with FRDA. One report detailed the outcomes of 17 pregnancies in women with FRDA, and identified pregnancy-induced hypertension as a complication in 11.8% of that cohort.[12] Another case report of a woman with FRDA reported the development of profound weakness and respiratory distress, secondary to the administration of magnesium sulfate to control preterm labor and preeclampsia.[13] In the present study, we retrospectively examined 31 women with FRDA who experienced 65 pregnancies resulting in 56 live offspring.

Materials and Methods

This study had the approval of the institutional review boards of our hospital and university. All subjects provided written informed consent before taking part in the study. The study was open to any woman with FRDA age >18 years who had at least 1 pregnancy, including those that ended in miscarriage. Subjects were recruited through our FRDA program and by word of mouth. At the time of study recruitment, there were roughly 140 patients, approximately equally divided by gender, followed up through the program.

We retrospectively interviewed 33 women; 2 women were excluded from data analysis because their diagnosis of FRDA could not be confirmed through medical documentation. Each subject filled out a questionnaire detailing her experience with pregnancy. The questionnaire focused on 2 overall aspects: (1) medical concerns and complications associated with pregnancy; and (2) psychosocial factors influencing the decision to have a baby. Specific questions detailed past and present medical his-

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TABLE 1
Cohort demographics at time of study participation

Characteristic	Women
Married	84%
Children reside with mother full time	77%
Reside on East Coast	52%
Reside with partner	88%
Perform all or most childcare	55%
Unemployed	61%
Nonambulatory	61%

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tory, age of FRDA diagnosis, history of pregnancies and deliveries, and feelings about pregnancy relating to FRDA. The questionnaire included both open- and closed-ended questions, as well as ranked items employing the Likert scale.

Two versions of the questionnaire were administered: one for women who were diagnosed with FRDA prior to their first pregnancy, and a second for women diagnosed after their first pregnancy. The questionnaires were nearly identical, except the former asked questions about how FRDA influenced the decision to become pregnant, and the latter asked questions about changes the women may have made knowing the FRDA diagnosis before pregnancy. For women unable to complete the questionnaire (for reasons such as inability to write), the study coordinator administered the questionnaire verbally. Obstetric medical records were obtained and reviewed for 19 of the women whose data are included in this study. For women with children age >18 years, it was not possible to obtain medical records from these pregnancies or births.

TABLE 2
Commonly reported health problems at time of study participation

Health problem	Women
Scoliosis	48.4%
Urinary incontinence	25.8%
Left ventricular hypertrophy	22.6%
Depression or anxiety	22.6%
Hypercholesterolemia	9.7%
Hypothyroidism	9.7%
Diabetes type 2	9.7%
Hypertension	6.5%
Diabetes type 1	3.2%
Ulcerative colitis	3.2%

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RESULTS

Cohort demographics

In all, 31 women were included in data analysis, all of whom resided in the United States and carried a confirmed clinical diagnosis of FRDA. Thirteen women (42%) were seen in the FRDA program. In the overall cohort, the mean length of the shorter GAA triplet repeat in the *FXN* gene was 421 repeats, with a minimum of 44 repeats and a maximum of 760 repeats. Two women carried point mutations (G130V and I154F). The average age of FRDA diagnosis was 24.4 years, and the average age at study participation was 38.2 years (Table 1). A total of 21 women (68%) were diagnosed with FRDA prior to their first pregnancy. The women had an average of 1.8 children each. The women also had a variety of health problems associated with FRDA[1,4,14] such as scoliosis, urinary incontinence, and left ventricular hypertrophy (Table 2).

Pregnancy data

In all, 31 women had a total of 65 pregnancies, including 1 twin gestation. Of those pregnancies, 55 resulted in 56 live-born children. Nine pregnancies (13.8%) ended in spontaneous abortion (SAB), a smaller percentage than the estimated national incidence.[15] Of that group, 4 women each experienced a SAB, 1 woman had 2 SABs, and 1 woman had 3 SABs. These occurred at an average of 8.17 weeks of gestation. There was no information in any of the medical records to suggest that the SABs were related to FRDA, and all the women had other term pregnancies. Additionally, a 36-year-old woman terminated a pregnancy at 16 weeks, following prenatal diagnosis of Trisomy 18, presumptively attributed to advanced maternal age.[16] This mother had no further pregnancies.

The average age of the cohort during first pregnancy was 25.7 years. In all, 22 women (70.9%) planned their first pregnancy. Of that group, the average time to get pregnant was 97.2 days. Eleven women (35.5%) requested their partner undergo FRDA carrier testing prior to conception. All of the women received regular obstetric care during pregnancy, with 4 (6.2%) pregnancies deemed high risk, 1 of which was considered high risk due to FRDA. In this case, the mother was nonambulatory and her physician believed she was at risk for the development of deep vein thrombosis. Thirteen women (41.9%) were followed up by a cardiologist during pregnancy. One woman was a type 1 diabetic prior to pregnancy and 1 woman developed gestational diabetes, which occurs in 4-8% of pregnancies.[17,18] Four women (12.9%) had abnormal glucose tolerance test results during pregnancy, but did not require pharmacologic intervention. For the 11 women on whom data were available, the average weight gain during pregnancy was 36.6 lb.

The women were asked to retrospectively rate if they believed pregnancy made the FRDA worse, better, or unchanged. Eight women (28.6%) believed pregnancy improved their symptoms, typically citing a feeling of improved balance and coordination. Ten women (35.7%) believed pregnancy made their symptomatology worse, most commonly experiencing increased fatigue, followed by urinary urgency, and further speech, balance, and coordination difficulties. The remaining women believed pregnancy did not alter their symptoms of FRDA.

Thirty women carried pregnancies to term, and of those, 20 women (66.7%) reported experiencing at least 1 complication during pregnancy (Table 3). The most common complication was preterm birth, identified in 12.96% of FRDA pregnancies. This rate is similar to the general population incidence.[19] Of those who experienced complications, 18 women (90%) believed them to be unrelated to FRDA.

Birth data

Of 54 live births on whom data were sufficiently complete, 42 were vaginal deliveries (77.8%) and 12 (22.2%) were cesarean sections, including 2 elective cesarean sections. The cesarean section rate was below the national average of approximately 25%.[20] In all, 47 babies (87.04%) were born at term, between 38-42 weeks of pregnancy. Seven babies (12.96%) were preterm, born between 35-37 weeks of pregnancy. The average birth weight of the babies was 7 lb, 7.5 oz; 48 babies (88.9%) weighed between 6 and 9 lb; 2 babies (3.7%) weighed <6 lb; and 4 babies (7.4%) weighed >9 lb. When available, the average Apgar score of the newborns was noted. Nine newborns had an Apgar score between 7 and 10 at 1 minute of birth, and 1 baby had an Apgar score between 4 and 6. All babies on whom data were available had an Apgar score between 7 and 10 at 5 minutes of birth.

The average length of the hospital stay for the mother following delivery was 2.6 days. Most babies (94.4%) went home from the hospital at the same time as their mothers. Three babies (5.6%) had longer stays. Of those babies, 1 was febrile and spent 2 days in the neonatal intensive care unit for transient tachypnea of the newborn. Another spent 10 days in the neonatal intensive care unit for respiratory distress syndrome complicated by a small pneumothorax of the left anterior lobe. Insufficient medical records were available to evaluate the cause of the prolonged hospitalization for the third infant.

The women were asked to retrospectively self-rate FRDA changes they experienced immediately following delivery. Fourteen women (50%) believed the FRDA symptomatology did not change. Two women (7.1%) believed that the FRDA improved following delivery, but could not specify the exact nature of improvement. Twelve women (42.9%) believed that the FRDA became worse following delivery, citing reasons such as increased fatigue, urinary urgency, and coordination and balance difficulties.

TABLE 3
Reported complications in 54 pregnancies/deliveries resulting in live births

Complication	FRDA cohort	General population
Preterm birth (35-37 wk)	12.96%	12%[19]
Fetal distress	7.4%	2%[26]
Hypotension	7.4%	10% (with maximum DBP ≤60 mm Hg)[32]
Breech presentation	7.4%	3-4%[27]
Preeclampsia	3.7%	5%[25]
Urinary tract infection	3.7%	4.7%[28]
Nuchal cord	3.7%	15%[28]
Second-trimester bilateral choroid plexus cysts on ultrasound	1.9%	1%[30]
Subchorionic hematoma	1.9%	4%[29]
Oligohydramnios	1.9%	1.7-7%[30]
Precipitous labor requiring home delivery	1.9%	Data unavailable
Gestational diabetes	1.9%	4-8%[17,18]
Hypertension	1.9%	5-7%[31]

DBP, diastolic blood pressure; *FRDA*, Friedreich ataxia.

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Psychosocial factors relating to pregnancy

Of those who were diagnosed with FRDA prior to their first pregnancy, 47.4% were concerned or extremely concerned that their FRDA symptoms would worsen with pregnancy. 57.9% were concerned or extremely concerned they would have trouble caring for their baby because of FRDA. In all, 52.4% of the women said FRDA had a huge or moderate impact on their decision to get pregnant. A total of 52.6% of the women were concerned or extremely concerned about a shortened life expectancy because of FRDA and had concerns about leaving their children without a mother.

Half of the women stated that their primary care physician was somewhat or totally supportive of their decision to become pregnant; 81.8% believed their obstetrician was somewhat or totally supportive of their decision. Those women who did not think their physician was supportive often recounted this experience as painful, including 1 woman who was told by her doctor to find someone else to care for her baby, as she would never be able to do so herself. All of the women with spouses believed they were somewhat or totally supportive of the pregnancy.

Of those who were diagnosed with FRDA at some point following their first pregnancy, 30% said they would not have had children in retrospect. These women feared their children would be made fun of for their mother's "ataxic gait" and believed their disease was a burden to their children. Other mothers with physical disabilities have provided similar descriptions, saying they went "to great lengths to present themselves and their children as managing normally in order to be accepted as ordinary mothers."[21]

As previous studies of mothers with physical disabilities have shown, many of the FRDA mothers had to make special accommodations for their babies.[22] One wheelchair-bound mother went crib shopping with a physical therapist to find a crib accessible at her height. Others experienced difficulty and fear carrying their babies due to their ataxia. Most struggled, at least minimally, with the physical aspects of their children's daily care. Many of the women believed it was easier to care for young children in the earlier stages of FRDA.

The majority of women believed their children benefited from having a mother with FRDA, stating their children were more sensitive and caring toward the needs of others, as has been previously demonstrated in studies of children whose parents are disabled.[23] Additionally, FRDA mothers believed their children saw more of the "big picture" of life and were able to "let trivial things go."

Comment

The above results suggest that women with FRDA are capable of successful pregnancy with relatively few complications. FRDA did not appear to increase the risk of SAB, preeclampsia, or preterm birth. Additionally, despite the sensory and proprioceptive loss that occurs in this disease, 77.8% of births were vaginal. The vast majority of babies were born at appropriate weights with no health complications.

The above results also suggest that individuals may experience varying degrees of pregnancy-related changes with FRDA. The women in the study were divided as to whether pregnancy made their FRDA symptoms worse, better, or unchanged. However, the results demonstrate that pregnancy does not necessarily make FRDA worse, as has been previously speculated. Additionally, the women were evenly divided as to whether FRDA stayed the same or became worse postpartum. Further research is needed with a larger cohort to determine the exact changes in FRDA that may occur during pregnancy and following delivery.

The present study is limited by the relatively small sample size of the cohort. However, due to the rare nature of FRDA, to the authors' knowledge, this is the largest population of FRDA women who have been studied with regard to pregnancy. Additionally, there may be some cohort bias, as most of the participants were recruited through a dedicated FRDA program or through word of mouth. Therefore, the sample may be biased toward a population already receiving specialized care for their disease, indicating a higher level of health than the overall FRDA population. In addition, the women included in this study had an average age of disease onset of 24.4 years and a mean GAA repeat of 421, which is commonly associated with a more moderate disease course. Therefore, the present results may be less applicable to the more traditional, severe form of FRDA, in which onset occurs in late childhood or early adolescence. With an earlier disease onset, patients typically become nonambulatory at younger ages and may experience increased cardiac, urinary, and neurologic dysfunction.

Additionally, this study asked women to rate their own impression of FRDA changes, using a subjective scale. Future studies could follow up women prospectively during pregnancy and measure FRDA changes on a validated, quantitative scale such as the FRDA Rating Scale. Finally, this study only includes 1 woman who terminated a pregnancy and did not give birth to any live children. FRDA women who had unsuccessful pregnancies may be less willing to participate in research such as this, and thus the results may not completely reflect the rate of pregnancy complications.

The present results suggest that pregnant FRDA women should be followed up closely, both by an obstetrician and a cardiologist; however, the pregnancy, under normal circumstances, likely need not be considered high risk. Additionally, although this study did not demonstrate an increased risk of gestational diabetes, FRDA patients in general are more predisposed to the development of diabetes.[1] Therefore, it is advisable that a mother's glucose levels be carefully monitored throughout pregnancy.

The above study highlights the importance of a physician who is supportive of the woman prior to and during her pregnancy. Previous studies of women with multiple sclerosis have emphasized the complex inner turmoil women with chronic diseases can experience when considering childbearing.[24] As more information on pregnancy with FRDA becomes available, it will be prudent to create decision aid materials to help educate women and their caregivers.

Lastly, when contemplating family planning, it may be advisable, when possible, for women to have children in the earlier stages of FRDA. As the disease progresses, it may become increasingly difficult for women to care for young children. Overall, our results suggest that women diagnosed with FRDA should be encouraged to proceed with pregnancy. ■

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