Clinical Management Guidelines for Friedreich Ataxia

Chapter 13. Family planning and pregnancy in Friedreich ataxia

Contents

This chapter of the Clinical Management Guidelines for Friedreich Ataxia and the recommendations and best practice statements contained herein were endorsed by the authors and the Friedreich Ataxia Guidelines Panel in 2022.

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13. Family planning and pregnancy in Friedreich ataxia

Lisa Friedman, Kimberly Schadt and David Lynch are acknowledged for much of the content of this chapter, taken from the previous version of the guidelines (2014).

Roger Peverill and Aarti Patel prepared the updated section on cardiac considerations and the corresponding recommendation (section 13.3).

This chapter covers the management of couples contemplating pregnancy and the prenatal and postnatal care of women with Friedreich ataxia, including the delivery of the baby and care following birth. This chapter largely comprises material from the 2014 guidelines, with the exception of the material related to cardiac considerations (section 13.3). In writing best practice statements and recommendations, the authors were tasked with answering the following questions:

For individuals with Friedreich ataxia what is the best management for pre-pregnancy counselling and family planning considerations? (see 13.2)

For women with Friedreich ataxia with heart failure what is the best management before and during pregnancy? (see 13.3)

For women with Friedreich ataxia what is the best management during pregnancy? (see 13.4)

For women with Friedreich ataxia what is the best management for other complications (besides heart failure) during pregnancy? (see 13.4)

For women with Friedreich ataxia what is the best management during delivery? (see 13.4)

For women with Friedreich ataxia what is the best management if anaesthesia is required during delivery? (see 13.4)

For women with Friedreich ataxia what is the best management during the post-partum period? (see 13.5)

13.1 Overview of family planning and pregnancy issues in Friedreich ataxia

With medical advances such as improved cardiac care and other medical interventions, the average life expectancy of individuals with Friedreich ataxia (FRDA) has significantly improved beyond the previously reported age of 37 years. As such, many females with FRDA are considering family planning and pregnancy. In a study by Friedman and colleagues (1), 52.4% of women said FRDA had a huge or moderate impact on their decision to get pregnant and 52.6% of women were concerned or extremely concerned about a shortened life expectancy because of FRDA. Many of the mothers in the study had to make special accommodations for their baby, such as buying wheelchair-accessible cribs. The majority of women felt that their children benefited from having a mother with a physical disability, saying their children were “more sensitive and caring towards the needs of others.”

This chapter provides specific guidance for practitioners caring for individuals with FRDA making this important decision. The 2014 guidelines were largely based on a retrospective study and several case reports of pregnancies in women with FRDA (1-5).

13.2 Planning for pregnancy

Women with FRDA can have uncomplicated pregnancies that do not necessarily lead to deterioration in disease-related symptoms, although this may at least partly reflect an inherent

selection bias in those who become pregnant (1). However, there are some specific considerations for a woman with FRDA and her partner when planning for pregnancy.

13.2.1 Carrier testing of reproductive partners

The availability of testing for carrier status of reproductive partners should be made known to couples where one member has FRDA. If testing is requested, the carrier status of the unaffected partner should be established prior to conception in order to advise the couple of the risk of having a child with FRDA and to offer appropriate counselling. Please refer to Chapter 11 for further discussion about genetic issues; in particular, carrier testing.

Timing of pregnancy

A retrospective review of 31 women with FRDA who experienced pregnancy found that it was easier for women in the earlier stages of the disease to care for children (1).

Best practice statements

Testing for carrier status of reproductive partners should be made available to couples where one member has Friedreich ataxia, prior to conception in order to advise the couple of the risk of having a child with Friedreich ataxia and to offer appropriate counseling.
When possible, it is advisable for women to have children earlier in their disease course.

13.3 Cardiac considerations for women planning for pregnancy

Roger Peverill and Aarti Patel

There is little data available about pregnancy in women with FRDA and reduced left ventricular ejection fraction (LVEF) who are either asymptomatic or have heart failure (HF) symptoms. Based upon data in other cardiac conditions (6), it should be assumed that there is a high risk of maternal and fetal complications in women with FRDA and either reduced LVEF or a history of HF; therefore, avoidance of pregnancy should be recommended in such individuals (7).

Women with FRDA and reduction in LVEF should be advised that pregnancy could result in cardiac decompensation and greater fetal risk and that it is therefore advised against. Pre-pregnancy counseling including consultation with a multidisciplinary team, including a cardiologist and an obstetrician, may assist in decision making.

Best practice statement

Pregnancy in women with Friedreich ataxia and a reduced left ventricular ejection fraction and/or a history of heart failure is likely to be associated with an increased risk of adverse maternal and fetal outcomes. Pre-pregnancy counseling for such women is suggested, including consultation with a multidisciplinary team that should include a cardiologist and an obstetrician.

Recommendation

Grading for strength of recommendation and level of evidence

For the rating of the **strength** of the recommendation, in addition to evidence from studies in FRDA, evidence from like conditions, clinical experience and expert consensus are taken into account when published evidence is not available.

The **level of evidence** is based on published evidence from studies in FRDA. If there is no published evidence in FRDA, evidence from other like conditions or clinical expertise may have been used to make the recommendation – this is graded as 'very low' or in some cases 'low' level evidence. See the table below for an explanation of the symbols used to grade recommendations.

Strength of recommendation	Symbol	Level of evidence	Symbol
Strong for intervention	↑↑	High	⊕⊕⊕⊕
Conditional for intervention	↑	Moderate	⊕⊕⊕◯
Neither intervention nor comparison	—	Low	⊕⊕◯◯
Conditional against intervention	↓	Very low	⊕◯◯◯
Strong against intervention	↓↓		

Women with reduced ejection fraction planning pregnancy

Should advice on avoiding pregnancy versus pursuing or not avoiding pregnancy be used for high risk pregnancy (patients with reduced ejection fraction with or without heart failure) with Friedreich ataxia?	**Strength**	**Level of evidence**
We conditionally recommend that women with Friedreich ataxia with reduced ejection fraction with or without heart failure be advised of the risks of mortality and morbidity associated with commencing or proceeding with a pregnancy.	↑	⊕◯◯◯
Justification: Women with Friedreich ataxia with reduced ejection fraction with or without heart failure are at significant risk of mortality and morbidity. Evidence for this is apparent from women with other (non-Friedreich ataxia-related) cardiomyopathies and associated reduced ejection fraction with or without heart failure.		
Subgroup considerations: This recommendation is for women with Friedreich ataxia with reduced ejection fraction with or without heart failure.		

Lay summary

Lay summary of clinical recommendation for planning pregnancy for women with Friedreich ataxia with reduced ejection fraction

Why this recommendation?

This recommendation suggests that women with Friedreich ataxia with reduced ejection fraction (that is where muscles of the left ventricle of the heart do not pump well) who are either contemplating pregnancy or are pregnant should be advised of the risks of significant health issues for them and their baby if they become pregnant or continue a pregnancy.

What does this mean for you as a person living with Friedreich ataxia or caring for someone living with Friedreich ataxia?

If you are thinking about becoming pregnant or you are already pregnant, it might be important for you to speak with your healthcare professional about Friedreich ataxia and pregnancy and what it means for you.

Who is this recommendation specifically for?

This recommendation is specifically for women with Friedreich ataxia and reduced ejection fraction with or without heart failure.

13.4 Management during pregnancy and delivery

13.4.1 Fetal and maternal outcomes in FRDA

Two studies have evaluated pregnancy in larger cohorts of women with FRDA. A short report by MacKenzie and colleagues (5) detailed 17 women with 17 pregnancies and a retrospective analysis by Friedman and colleagues (1) studied 31 women who had 65 pregnancies resulting in 56 live offspring. Findings from these studies are summarized below.

Spontaneous abortion occurred in 13.8% of the Friedman cohort (1), a smaller percentage than the estimated frequency in the United States of America (USA) (8). The spontaneous abortions occurred at an average of 8.2 weeks gestation. There was no information to suggest any of the spontaneous abortions were related to FRDA and all women who experienced spontaneous abortion in the Friedman cohort had other successful pregnancies.

Pre-term birth occurred in 13% of the Friedman cohort (1). This was defined as babies born before 37 weeks gestation. In this study, the earliest birth was 35 weeks (considered a late preterm). In the Mackenzie study (5), all babies were born later than 36 weeks gestation. In the general population (USA), the rate of preterm birth during a similar time period was about 12% (9). Thus, the rate seen in the Friedman study is largely comparable.

Impaired glucose tolerance occurred in 12.9% of the Friedman cohort (1) and 5.8% of the Mackenzie cohort (5). In each cohort, one woman developed gestational diabetes during pregnancy. The remaining women were managed with dietary modification. In the general USA population, the estimated incidence of gestational diabetes during pregnancy is reported to be as high as 18% (10). Thus, the numbers reported in women with FRDA appear to be lower than in the general population, although small sample sizes in the FRDA studies should be noted.

Pregnancy-induced hypertension occurred in 11.8% of the Mackenzie cohort (5) and 1.9% of the Friedman cohort (1). In the general population, the estimated incidence during pregnancy is between 5% and 7% (11).

Preeclampsia occurred in 3.7% of the Friedman cohort (1) and none of the Mackenzie cohort (5). In the general population, the estimated incidence during pregnancy is approximately 5% (12).

13.4.2 Surveillance during pregnancy

Glucose tolerance testing – Individuals with FRDA are predisposed to the development of diabetes. Therefore, it is advisable that a woman's glucose levels be carefully monitored throughout pregnancy. As is standard with any pregnancy, glucose tolerance testing should be performed between 24-28 weeks of gestation (13) or earlier for individuals deemed to be at high risk by their health practitioner.

Cardiac management – Individuals with FRDA are predisposed to the development of cardiomyopathy, arrhythmias and other cardiac abnormalities. Thus, close monitoring by a cardiologist during pregnancy is essential.

Neurologic exam testing – Changes in the patient's FRDA disease status can be monitored prospectively by a trained physician using the Friedreich Ataxia Rating Scale (FARS) exam or another

suitable neurologic exam. This will allow for quantitative tracking of the neurologic disease changes that occur with pregnancy. One would not anticipate permanent changes in neurologic disease status as a direct result of pregnancy; however, women may experience transient changes which should be monitored and followed by a physician to assure that level of functioning and disease status return to pre-pregnancy state.

13.4.3 Friedreich ataxia-related changes with pregnancy

In the Friedman and colleagues study (1), women were asked to retrospectively rate the changes in their FRDA they perceived during pregnancy: 7.1% of women felt pregnancy made their disease better, citing a feeling of improved balance and coordination; 42.9% of women felt pregnancy made their FRDA worse, most commonly experiencing increased fatigue, urinary urgency, speech, balance and coordination difficulties; 50% of women felt pregnancy did not alter their FRDA.

13.4.4 Planning for caring for the infant

During pregnancy consideration should be given to the requirements of caring for a baby post-partum, including any adaptions of the environment that may be required to facilitate safe and effective care of the infant. Consultation with allied health clinicians regarding equipment requirements and/or specific techniques related to caring for the baby may be of benefit (14).

13.4.5 Management of complications during pregnancy

As described above, complications of pregnancy may arise and need to be managed appropriately. Several case reports detail specific management considerations for women with FRDA.

Preeclampsia

One case study by Bruner and colleagues (3) described profound motor weakness and respiratory depression precipitated by the use of magnesium sulfate to treat preeclampsia. The authors hypothesized that magnesium may act synergistically with the underlying neuromuscular abnormalities found in FRDA to cause acute profound weakness. An alternative treatment may be phenytoin (2), although this has not been tried in any studies to date.

Pre-term labor

Although beta-agonist tocolytic agents are often used in an attempt to arrest early labor, these agents may be problematic in women with FRDA due to underlying cardiac and/or endocrine pathologies. Some experts have speculated that Indomethacin may be one potential alternative although no research exists on this topic to date (2).

Deep vein thrombosis

One case study detailed the development of deep vein thrombosis (DVT) in a 23-year old gravida 3 para 1 female with FRDA at 34 weeks gestation (2). The patient was treated with enoxaparin but went on to develop a pulmonary embolism. She had spontaneous vaginal delivery at 38 weeks. Upon birth, her infant was found to have two ventricular septal defects and coarctation of the aorta, which required surgical correction. The authors stress that during pregnancy, heparin is the mainstay of treatment for DVT as Coumadin (warfarin) crosses the placental membrane and is a known teratogen.

13.4.6 Management during delivery

In the Friedman cohort (1), 78% of births were vaginal, while 22.2% were cesarean sections, including two elective cesarean sections. The cesarean section rate was below the national average in the USA of approximately 25% (15). In the Friedman study, 87% of babies were born at term, with 13% born pre-term (between 35 and 37 weeks).

In the Friedman cohort (1), the average birth weight of the babies was 7 lb 7.5 oz (3390 g), with 88.9% of babies born normal weight (defined as between 6 and 9 lbs (2720 to 4080 g). Ninety per cent of newborns had an Apgar score between 7 and 10 at one minute after birth. All babies on whom data was available had an Apgar score between 7 and 10 at 5 minutes after birth.

From the Friedman cohort (1), the average length of hospital stay for the mother following delivery was 2.6 days and 94.4% of babies were discharged from the hospital with their mothers. Three babies had longer stays: one was febrile and spent two days in the NICU for transient tachypnea of the newborn; another spent 10 days in the NICU for a small pneumothorax. Insufficient medical records were available to evaluate the cause of the third infant's prolonged hospitalization. At the time of this study, in the USA, following uncomplicated deliveries it was standard for mothers and infants to remain hospitalized for 48 hours following a vaginal delivery and 96 hours following a caesarean section (16). Thus, the outcomes seen in women with FRDA follow the expected time trajectory.

Fetal distress was found as a complication in 7.4% of laboring mothers in the Friedman cohort (1). In the general population, it is reported to be approximately 2% (17). The reason for the elevation among the babies of women with FRDA is unclear. However, during delivery, it is imperative that the baby be closely monitored.

Despite the sensory and proprioceptive loss that occurs in FRDA, a vaginal delivery can still be expected of most pregnancies. The vast majority of babies born to mothers with FRDA are at healthy birth weights and can be expected to be discharged home with their mothers following the traditionally recommended length of stay (48 hours for vaginal delivery, 96 hours for caesarean section). As women with FRDA are potentially at higher risk for fetal distress during delivery, close fetal monitoring during this stage is imperative.

Management if anesthesia is required during delivery

There are reports of the successful administration of both epidural and spinal anesthesia to women with FRDA during delivery (4, 5).

Best practice statements

Women with Friedreich ataxia should be encouraged to proceed with pregnancy if they wish to do so and if their cardiac status is adequate (18).
Glucose tolerance testing should be performed between 24 and 28 weeks of gestation or earlier for individuals deemed to be at high risk by their practitioner (13).
Women with Friedreich ataxia should have close monitoring by a cardiologist during pregnancy.
There is insufficient evidence to determine if magnesium sulfate can be safely administered to women with Friedreich ataxia with preeclampsia.
There is insufficient evidence to determine if common beta-agonist tocolytic agents can be safely administered to women with Friedreich ataxia experiencing pre-term labor.

Pregnant women with Friedreich ataxia and deep venous thrombosis should be treated with heparin as opposed to warfarin (2).
Vaginal delivery can be expected for most pregnancies in women with Friedreich ataxia (1).
Close fetal monitoring during delivery is recommended (19).
If cesarean section is medically indicated, epidural or spinal anesthesia can generally be safely used in women with Friedreich ataxia (4, 5).

13.5 Management during the post-partum period

Despite the sensory and proprioceptive loss that occurs in FRDA, a vaginal delivery can still be expected of most pregnancies and under normal circumstances, the pregnancy of a woman with FRDA need not be considered high risk. The vast majority of babies born to mothers with FRDA are of healthy birth weights and can be expected to be discharged home with their mothers following the traditionally recommended length of stay (48 hours for vaginal delivery, 96 hours for caesarean section).

Women may experience some physical de-conditioning as a result of their pregnancy; hence it is important for the woman to re-engage with their physical therapy regime as soon as medically appropriate after delivery.

See Chapters 3.2 and 3.3 for further information on physical therapies.

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