REVIEW ARTICLE

Sjögren Syndrome and Pregnancy: A Literature Review

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ABSTRACT

Objectives: Autoimmune diseases do not impair fertility, and women with autoimmune diseases who become pregnant are likely to experience more complicated pregnancies than are women without the disease. Pregnancies complicated by these disorders have a high clinical impact on both the pregnancy and the disease. The effect of autoimmune disease on pregnancy differs according to the type of maternal disease, disease activity, severity of organ damage, antibody profile, and drug treatment. Sjögren syndrome is an autoimmune disease with a high prevalence of anti-SS-A (anti-Ro) and anti-SS-B (anti-La) antibodies. Anti-SS-A antibodies are associated with congenital heart block. Data on pregnancy outcomes in primary Sjögren syndrome are scarce.

Methods: We performed a review of the literature regarding pregnancy outcomes in women with Sjögren syndrome.

Results: Women with Sjögren syndrome are likely to experience more complications during pregnancy than women without an autoimmune disease. Studies show a high incidence of poor fetal outcomes for these patients.

Conclusion: Women with Sjögren syndrome require prenatal counseling explaining the risks involved and the need to control the disease well before conception. High-risk pregnancies can be optimally managed by a multidisciplinary team.

INTRODUCTION

Sjögren syndrome is an autoimmune disease that can present either alone, as in primary Sjögren syndrome (pSS), or in association with an underlying connective tissue disease, most commonly rheumatoid arthritis or systemic lupus erythematosus (secondary Sjögren syndrome).[1] The spectrum of clinical presentation of Sjögren syndrome extends from dryness of the main mucosal surfaces to systemic involvement (extraglandular manifestations). Dryness of mucosal surfaces occurs because of immune-mediated inflammation causing secretory gland dysfunction.[2] Sicca features primarily affect the quality of life, whereas the disease prognosis is marked by systemic involvement.[3] Sjögren syndrome is known to occur predominantly in women. Affected women are likely to experience more complicated pregnancies than are women without the disease.[4,5]

The effect of autoimmune disease on pregnancy differs according to the maternal disease, disease activity, severity of organ damage, antibody profile, and drug treatment.[6] Data on pregnancy outcomes in pSS are scarce, and results have been conflicting. Only a few studies have evaluated the pregnancy and fetal outcomes in patients with Sjögren syndrome. This prompted us to perform a review of the literature on the effect of Sjögren syndrome on pregnancy and fetal outcomes compared with those in the general obstetric population.

REVIEW OF LITERATURE

Epidemiology

Sjögren syndrome is one of the most common autoimmune diseases, with a reported prevalence between 0.1% and 4.8% in various populations when defined strictly according to the American-European Consensus Criteria.[7] It may occur at any age but affects mainly women at the fourth decade of life; the female-male ratio is estimated at 9:1.[8] The increasing frequency rate of pregnancies in women with pSS and hence the increased impact of the disease on pregnancies complicated by it can be explained by these epidemiologic data and the prevailing recent social trend toward late marriages and advanced maternal age at the time of first pregnancy or increased interval between marriage and conception.

Pathophysiology

The histologic hallmark of the disease is the focal lymphocytic infiltration of the exocrine glands. Laboratory diagnosis of Sjögren syndrome is usually made by the following markers: antinuclear antibodies (most frequently detected), anti SS-A (also called anti-Ro; most specific), anti-SS-B (also called anti-La), and cryoglobulins and hypocomplementemia (main prognostic markers).[9] These markers mediate the tissue damage and are thus responsible for complications in pregnancies of women with Sjögren syndrome. These antibodies cross the placenta beginning at approximately 12 weeks of gestation and may exert the following effects on the fetal tissues: 1) inducing myocarditis; 2) binding apoptotic cells, blocking presumed physiologic clearance, and diverting clearance to macrophages; and 3) producing arrhythmia.[10,11]

Clinical Manifestations

Effect of Pregnancy on Sjögren Syndrome

Sjögren syndrome is likely to worsen during pregnancy and more so in the postpartum period. This is because the disease is sometimes complicated by pulmonary hypertension, which frequently worsens during pregnancy and in the postpartum period.

Effect of Sjögren Syndrome on Pregnancy

Women with Sjögren syndrome are likely to experience more complications during pregnancy compared with those without the disease. Pregnancy outcomes in women with Sjögren syndrome

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have not been extensively studied. Several studies have reported an increased rate of spontaneous abortion and fetal loss associated with Sjögren syndrome (Table 1).[4,12-14] This may be explained by, first, the usually older age of the patients at the time of conception and, second, a possible immunologic factor involved in the mechanisms of miscarriage.[14]

Various studies have demonstrated an extremely variable rate of induced abortions, depending on the counseling given about the fetal-maternal risks and the socioeconomic status of the patient (Table 1).[5,14-17] A significant increase in the rate of preterm deliveries was found in pregnant women with pSS in most of the studies.[16,17] The mean neonatal birth weight was significantly lower in the offspring of women with pSS. This may be related to a pathologic intrauterine growth restriction and is not influenced by the timing of the delivery.[13] An increased frequency of cesarean delivery was observed in patients with Sjögren syndrome.[17] This might be caused by an increased risk of severe fetal outcomes in pregnancies in the Sjögren syndrome population resulting from an increased risk of fetal growth restriction.

Well-known fetal outcomes in Sjögren syndrome-complicated pregnancies are neonatal lupus and congenital heart block (CHB).[18] CHB is the most severe fetal complication and supposedly occurs because of the damage of the atrioventricular node by anti-SS-A or anti-SS-B antibodies, or both. The reported prevalence of CHB in the offspring of an anti-SS-A-positive woman is 1% to 2%. The recurrence rate in a patient with antibodies, who has a previous child affected, is approximately 10 times higher.[19-21] The incidence of neonatal lupus in an offspring of a mother with anti-SS-A antibodies is estimated at approximately 1% to 2%.[22]

DISCUSSION

Management

The outcome of pregnancies in women with Sjögren syndrome can be excellent with use of a multidisciplinary management approach involving an obstetrician who specializes in high-risk pregnancies, a rheumatologist, and a pediatrician.[11]

Prenatal Management

Women with Sjögren syndrome planning to conceive must undergo good counseling regarding all specific risks and complications involved, medications that are contraindicated during pregnancy, and whether the patient is in the best condition to get pregnant according to underlying disease activity and complications. Ideally, the disease should be well under control three to six months before conception.

Antenatal Management

One of the most dreaded complications of pregnancy in patients with Sjögren syndrome is CHB. A woman is at risk of delivering a baby affected by CHB if she is anti-SS-A positive.[11] Frequent surveillance by serial echocardiograms and obstetric sonograms between 16 to 20 weeks of gestation and thereafter is required for at-risk pregnancies. The goals are early diagnosis and early treatment of incomplete CHB, thus improving the outcome for the fetus.[23] The rationales for management are 1) to decrease maternal autoantibodies and then to decrease their placental transfer and 2) to decrease the inflammation once it occurs before it leads to permanent fibrosis and irreversible CHB.[24] Maternal treatment with fluorinated corticosteroids such as dexamethasone or betamethasone, can reduce the antibody-mediated inflammatory damage of nodal tissue because they are not inactivated by placental hydroxylase.[25] However, there is no definite evidence about whether steroids effectively decrease the titers of anti-SS-A or anti-SS-B antibodies or reverse the CHB.[25-27] However, dexamethasone has been reported to reverse carditis and incomplete CHB, and to improve fetal hemodynamics.[23,25,27-29] Hence, dexamethasone treatment is recommended if the block is recent or incomplete, or if there is evidence of cardiac failure.[25,30,31] Maternal risks of fluorinated steroids include infection, osteoporosis, osteonecrosis, and glucose intolerance. Specific fetal risks include intrauterine growth restriction, oligohydramnios, and possibly adrenal suppression.[31] The alternative therapies, as evidenced by a few case reports, include plasmapheresis,[31] intravenous immunoglobulins, and

Table 1. Pregnancy outcomes in women with Sjögren syndrome

Author	Study design	Pregnancies, no.	Spontaneous abortions, no. (%)	Still births, no. (%)	Induced abortions, no. (%)	IUGR, no. (%)	Premature deliveries, no. (%)	Live births, no. (%)	Congenital heart block, no. (%)
Skopouli et al,[5] 1994	Retrospective study with questionnaire	207	18 (9)	3 (1.5)	75 (36)	NR	2(1)	111 (54)	2 (1)
Siamopoulou-Mavridou et al,[4] 1988	Retrospective study with questionnaire	63	13 (21)	2 (3)	NR	NR	0	48 (76)	NR
Julkunen et al,[12] 1995	Retrospective study with records and interview	55	10 (18)	1 (2)	NR	1 (2)	1 (2)	44 (80)	NR
Priori et al,[16] 2013	Case-control delivery registry linkage study	45	4 (9)	0 (0)	1 (2)	NR	6 (13)	40 (89)	2 (4)
Takaya et al,[15] 1991	Retrospective study with questionnaire	39	2 (5)	0 (0)	9 (23)	NR	1 (3)	28 (72)	NR
De Carolis et al,[13] 2014	Electronic case records review	34	10 (29)	0 (0)	1 (3)	1 (3)	9 (27)	23 (68)	2 (6)

IUGR = intrauterine growth restriction; NR = not reported.

β-sympathomimetics.[32] In most cases, complete heart block requires a pacemaker implantation in the infant, preferably in the neonatal period.[11]

CONCLUSION

Women with Sjögren syndrome are likely to experience more complications during pregnancy. Studies show a high incidence of poor fetal outcomes for these patients. Women with this underlying autoimmune disorder must undergo prenatal counseling explaining all the risks involved and the need to control the disease well before conception. These high-risk pregnancies can be optimally managed by a multidisciplinary approach involving a high-risk obstetrician, a rheumatologist, and a pediatrician. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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