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Pregnancy and autoimmune connective tissue diseases

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A B S T R A C T

Autoimmune connective tissue diseases predominantly affect women and often occur during the reproductive years. Thus, specialized issues in pregnancy planning and management are commonly encountered in this patient population. This chapter provides a current overview of pregnancy as a risk factor for onset of autoimmune disease, considerations related to the course of pregnancy in several autoimmune connective tissue diseases, and disease management and medication issues before pregnancy, during pregnancy, and in the postpartum period. A major theme that has emerged across these inflammatory diseases is that active maternal disease during pregnancy is associated with adverse pregnancy outcomes, and that maternal and fetal health can be optimized when conception is planned during times of inactive disease and through maintaining treatment regimens compatible with pregnancy.

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Autoimmune connective tissue diseases (CTDs) are associated with strong female preponderance, and often present before or during the reproductive years [1]. As such, specialized issues in pregnancy planning and management are commonly encountered in this patient population, which includes rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), antiphospholipid antibody syndrome (APS), systemic sclerosis (SSc), primary Sjogren's syndrome (PSS), and inflammatory myositis. For decades, women particularly with SLE were advised against pregnancy given the high rates of observed poor outcomes, concern for disease flare, and lack of evidence for safe treatment options. Indeed, women with SLE/APS especially have higher rates of preeclampsia, intrauterine growth restriction (IUGR), and prematurity [2–4]. However, with advances in disease management, pregnancy outcomes in these populations have improved, and increasingly more women with CTDs are choosing to attempt pregnancies [5]. Furthermore, interesting research in the field is leading to identification of predictors for high-risk pregnancies, which will increasingly allow for a personalized approach to pregnancy management. An emphasis on preconception counseling and tight disease control in the months leading up to conception are essential components of this new era of pregnancy and CTDs. Equally important is the recognition that untreated disease in pregnancy is associated with risks to both the mother and child [6], and the preponderance of evidence demonstrates the importance of continuing medications that prevent active disease and that do not harm the baby throughout pregnancy. A thorough understanding of the range of therapeutic options available for treatment during pregnancy is therefore essential, and has expanded in recent years to include monoclonal antibody therapy. In this context, and with increasing accrual of follow-up data for children born to mothers with CTDs, the best practices for management of these pregnancies are evolving rapidly.

Pregnancy and subsequent risk of autoimmune CTDs

Whether pregnancy is a risk factor for the development of new-onset autoimmune CTD remains an open question. Among the rheumatic diseases, RA has perhaps received the most attention on this topic. As reviewed elsewhere, a significantly decreased risk of RA has been described in several retrospective studies in women who have ever been pregnant compared to nulliparous women [7–10], whereas a number of other studies, including population-based cohort studies, have not detected an association between parity and subsequent risk of RA [11–16]. Conflicting results have been reported in other diseases such as SLE and SSc, also reviewed elsewhere [17].

Notably, a large population-based Danish study examining the autoimmune diseases as a group found that risk of developing maternal autoimmune disease significantly increased during the first year post partum, but it subsequently trended in the opposite direction [18]. Onset of RA has particularly been described to occur with increasing frequency during the postpartum period. In fact, a 1953 study concluded that “The onset of rheumatoid arthritis during pregnancy or immediately after it is so common that in certain circumstances pregnancy can be regarded as an aetiological factor” [19]. A 1992 British case–control study found a reduced incidence of onset of RA during pregnancy, but the highest postpartum increase was also observed during the first 3 months post partum (OR 5.6) and remained elevated during the subsequent 9 months [20]. A 1993 case–control study from the Netherlands reported similar trends [21]. Together, these studies underscore the importance of delineating time windows in relation to pregnancy, and they suggest that the postpartum period warrants special consideration in terms of risk of autoimmune diseases among women.

Pregnancy considerations in autoimmune CTDs

Systemic lupus erythematosus

SLE (or “lupus”) affects females in a 9:1 ratio to males [22,23], with a 2.5-fold increase in prevalence among African-Americans [24]. The adverse pregnancy outcomes observed with lupus are well known, and include increased rates of IUGR, preterm birth, and fetal loss, as well as the syndrome of neonatal lupus (NL), associated with the transplacental passage of autoantibodies, discussed below. A 2006 study using the Nationwide Inpatient Sample in 2002 comparing CTD pregnancies to control pregnancies revealed significantly higher rates of hypertensive disorders (odds ratio (OR) 3.3 (95%