Systemic Lupus Erythematosus: Pathogenesis, Clinical Manifestations and Diagnosis

In-Depth Discussion I

Pregnancy in Systemic Lupus Erythematosus

Systemic lupus erythematosus (SLE) is the autoimmune disease that most commonly compromises pregnancy. In recent years, however, there has been a great change in the perception of the effects of pregnancy on SLE flares and of SLE on pregnancy outcome (both fetal and maternal). Because of important advances in the obstetric care and medical evaluation and treatment of women with SLE, many improvements in their pregnancies have occurred.

Influence of Pregnancy on SLE

At present, as therapy has helped more SLE patients to feel well enough to have families, the topic of the influence of pregnancy on SLE is a matter of great interest. However, there is no agreement about the exact influence of pregnancy on the course of SLE. Thus, several prospective and retrospective recent studies, including some reports using a matched-non pregnant control design (1-4), have shown contradictory results, with a reported frequency of lupus flare ranging from 13 to 60%. This wide range in lupus flare during pregnancy among different studies may be explained by several factors such as different entry criteria, methodological differences in the study design, small number of patients included, criteria used to diagnose and quantify flare, and routine steroid administration. Additionally, there could be many difficulties in the differential diagnosis between SLE flare and some pregnancy symptoms (facial rash, arthralgia, fatigue, edema in the legs) as well as between renal flare and preeclampsia. In our experience, the frequency of lupus flare is about 23.3% or 0.004 per patient/month. Furthermore, most flares are mild and mainly cutaneous (54.1%) (5).

In most of these patients, the disease was clinically inactive at conception and this fact may explain the discrepancy with studies including a predominance of patients with more severe and chronic manifestations of SLE and showing flare rates as high as 60%.

The use of prophylactic steroids during pregnancy is a matter of controversy. Some authors recommend the use of prednisone throughout pregnancy for all pregnant lupus patients (1) but others disagree (3). Our results show that the majority of SLE flares (46.6%) occurred during late pregnancy or the postpartum period despite that, initially, most women were prophylactically given prednisone from 36 weeks pregnancy until 1 month after delivery, thus suggesting that prednisone does not prevent lupus flare and causing us to abandon such practice in 1995.
We consider that pregnancy does not cause SLE to worsen, provided that patients are clinically inactive at conception and managed according to a careful multidisciplinary monitoring and treatment schedule. This contention is also supported by experimental evidence showing that pregnancy, parturition and suckling have no negative effects on variables of disease activity in the mouse model of SLE (6). Therefore, patients should be advised to become pregnant when the disease is inactive, strict obstetrical/medical care should be performed during pregnancy and, although prophylactic steroids are not required, several drugs, such as hydroxychloroquine, prednisone and azathioprine, can be safely used in case of SLE flare.

INFLUENCE OF SLE ON PREGNANCY

Studies in the sixties reported that SLE pregnancies were clearly associated with increased rates of obstetric and neonatal complications. At present, it is well known that women with SLE at increased risk for pregnancy loss are those having antiphospholipid antibodies (aPL). With the widespread use of careful monitoring and treatment schedules for these patients, many improvements in both fetal and maternal pregnancy outcomes have occurred. The current incidence of spontaneous abortion (11.7%) (5) is comparable to recent accurate estimates of pregnancy outcomes in a general obstetric population (7).

Reported incidences for preterm delivery in SLE pregnancies have ranged between 17% and 49% in recent studies (8). This apparent discrepancy may be explained by the different definitions (36, 37 and even 38 weeks) used in the different studies and by the fact that preterm birth in SLE is multifactorial. Lupus activity and hypertension are the strongest predictors of preterm birth. Seventeen of 91 viable pregnancies (18.7%) ended before 37 completed weeks in our series (5), mainly because delivery was induced or caesarian section was performed in patients with aPL and abnormal fetoplacental Doppler flow kinetics.

Pregnancies in women with SLE are recognised to result in excessive perinatal morbidity and mortality. There were five perinatal deaths in our series (4.9%): Three cases due to extreme prematurity, one due to congenital heart block and one intrauterine death (5). This figure is similar to those reported in other recent prospective studies (3,4) and lower than those observed in early retrospective studies on SLE and pregnancy. In this regard, it is noteworthy that prospective studies represent more recent pregnancies and improvements in obstetric care and medical evaluation and treatment of SLE may be changing the natural history of lupus pregnancy.

Also, more recent prospective studies may include a different selection of patients with SLE than those included in retrospective studies, mainly those with less severe disease. Additionally, it is of interest to note the low prevalence of congenital heart block due to the passive transfer of anti-Ro/SS-A or anti-La/SS-B antibodies from the mother.
Conflicting results have been reported regarding the prophylactic use of dexametasone in these cases, but careful monitoring of fetal heart activity with fetal echocardiography should be performed in order to obtain an early detection of congenital heart block and to place a pacemaker if required.

The influence on pregnancy of two SLE complications deserve especial attention: the existence of an associated antiphospholipid syndrome (APS) and of lupus nephropathy.

**Influence of the APS on pregnancy**

It is now well established that the presence of aPL, namely the lupus anticoagulant (LA) and anticardiolipin antibodies (aCL), are important risk factors for abortion in both SLE and non-SLE patients. Experimental and clinical evidence clearly favours the use of antiaggregant/anticoagulant agents, mainly aspirin and heparin, to prevent aPL-associated miscarriages (9). This topic is reviewed in depth in the module devoted to the APS.

**Influence of lupus nephropathy on pregnancy**

A history of renal involvement has been considered to be dangerous for gestation. Fifty percent of our pregnant patients with pre-existing renal disease developed hypertension and one of them also developed significant proteinuria, a typical feature of preeclampsia (10). This is in agreement with previous reports showing such an association. However, the rate of prematurity was similar between patients with and without previous renal involvement and most of our patients had good obstetrical outcome and none of them presented renal function impairment during or after pregnancy. Thus, in our experience, pre-existing lupus renal involvement is a risk factor for hypertension, but it does not contraindicate pregnancy if, similarly to the case of other pre-existing SLE manifestations, planning of conception is performed when nephropathy is not active and no therapeutic agents that can be teratogenic (i.e. cyclophosphamide) are used.

**FINAL REMARKS**

Pregnancy in patients with SLE should not be regarded as an unacceptable high risk condition for the mother or her baby provided that careful planning of conception and multidisciplinary monitoring and treatment are carried out.
REFERENCES


