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ORIGINAL ARTICLE

Pregnancy outcome in patients with systemic lupus erythematosus: A single center study in the High Risk Pregnancy unit

Eman Aly Hussein Aly [a,*], **Rafaat Mohamed Riyad** [a], **Abeer Nabil Mokbel** [b]

[a] *Department of Obstetrics and Gynecology, Kasr AL Aini Hospital, Cairo University, Egypt*
[b] *Department of Rheumatology and Rehabilitation Cairo University, Egypt*

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KEYWORDS

Systemic lupus erythematosus;
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Abstract *Background:* Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease that mainly affects females in the reproductive age.

Objective: To investigate pregnancy course and outcome in females with SLE, to evaluate the effect of pregnancy on SLE disease activity and to investigate the predictors of adverse pregnancy outcomes.

Methods: A prospective study of 91 pregnancies (84 women) with SLE. Comparisons were done using Chi-square test to evaluate the impact of clinical and laboratory parameters on maternal and fetal outcomes. Logistic regression analysis was used to study the predictors of adverse pregnancy outcome (defined as the occurrence of abortion, pre-eclampsia, prematurity, IUFD or SLE flare).

Results: The most common maternal manifestations of SLE were cutaneous lesions (93%), articular (92%), lupus nephritis (53%), hypertension (39%) and secondary antiphospholipid syndrome (APS) (38%). The incidence of abortion was (15%), IUGR (32%), prematurity (13%), pre-eclampsia (12%), IUFD (8%), NICU (15%), and LBW (22%). SLE antenatal flares were (44%), with 70% occurring in the second trimester, with renal flares being the most commonly reported (21%). The incidence of postnatal flares was 7%. There was significant association between hypertension and abortion ($p = 0.04$), pre-eclampsia ($p = 0.0001$) and SLE flares ($p = 0.0001$). Lupus nephritis and hypertension were predictors of preeclampsia ($p = 0.01$ and $p = 0.002$ respectively) and SLE flares ($p = 0.048$ and $p = 0.003$ respectively). Secondary APS and aCL IgG were also predictors of abortion ($p = 0.001$ and $p = 0.04$ respectively).

* Corresponding author at: Department of Obstetrics and Gynecology, Kasr EL Aini Hospital, Cairo University Hospitals, Egypt. Tel.: +20 2 33352214, +20 122 3518488.
E-mail address: emanalyhussein@yahoo.com (E.A. Hussein Aly).

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Conclusion: Careful monitoring of pregnancy and efficient treatment of SLE can decrease the risks for the mother and the fetus. However, despite improvements in pregnancy outcome of SLE pregnant patients, adverse maternal and fetal outcomes may occur. SLE may flare-up with pregnancy.

Introduction

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease that mainly affects females in the reproductive age group. Women with SLE have the same fertility rate as the age-matched population of healthy women (1). Historically, the general recommendation was against pregnancy in SLE patients due to poor fetal and maternal outcomes (2). However, over the past few years, the improved treatment allowed better control over the disease activity resulting in a remarkable improvement in the quality of life of these patients, including pregnancy outcomes (3). Nevertheless, there is still a considerable risk of fetal and maternal complications (4). Pregnancies for patients with SLE pose a greater risk of fetal loss, intrauterine growth restriction (IUGR), prematurity, pre-eclampsia, and low birth weight (LBW) (5,6).

Several studies discussed the impact of pregnancy on maternal lupus with conflicting results, where some studies showed increased SLE flares during pregnancy (7), while others found no difference in flares between pregnant and non-pregnant patients with SLE (8,9). The aim of this study was to evaluate the maternal and fetal outcomes of pregnancy in women with SLE, trying to investigate the predictors of adverse pregnancy outcomes and also to compare the results of the work done in our department with the current literature.

Patients and methods

This was a prospective study of 91 pregnancies in 84 SLE female patients attending the antenatal clinic at the High Risk Pregnancy unit in the Gynecology and Obstetrics Department at Cairo University Hospitals from October 2010 to January 2015. Each pregnancy was counted as a separate case. The study was approved by the Institutional Review Board. All patients were consented to participate in the study. All SLE patients fulfilled at least 4 of the 11 criteria of the American College of Rheumatology (10). Any pregnancy in a patient with active disease or before 6 months of SLE remission was excluded. Antiphospholipid syndrome (APS) was diagnosed according to the recent classification criteria (11). Management of patients in the study involved a multidisciplinary approach including obstetrics and a rheumatology team in addition to nephrology team for patients with renal involvement. Other specialties were considered as needed.

All patients were followed-up since diagnosis of pregnancy till delivery. Follow-up during postpartum period continued for 6 weeks. During the antenatal follow-up, pregnant women were seen once a month during the first trimester, every three weeks in second trimester, then twice weekly starting from the 28th week of pregnancy, and weekly starting from the 36th week. Patients were seen twice during postpartum period.

Thorough history taking, clinical examination and laboratory assessment were done for all patients. Data recorded included age at SLE diagnosis, duration of illness, previous and current SLE manifestations, current and past medications utilized, and laboratory data. At each visit, clinical evaluation of pregnancy and SLE current condition was performed. Investigations included antinuclear antibodies (ANA), anti-double stranded (dsDNA) antibodies, lupus anticoagulants (LAC), anticardiolipin antibodies via immunoglobulins G (aCL IgG) and M (aCL IgM). Anti-Ro/SSA and anti-La/SSB antibodies were also done. Baseline routine laboratory tests (followed by monthly follow-up tests) included complete blood picture, serum transaminases, alkaline phosphatase serum albumin, creatinine, urine analysis, 24-h urine collection for total proteinuria, Fasting and postprandial blood glucose, serum uric acid and erythrocyte sedimentation rate.

Antenatal ultrasound and Doppler scans for fetal assessment were regularly performed with detailed fetal anomaly scan at 22 weeks of gestation. Fetal echocardiography was performed in all patients with anti-SSA and/or anti-SSB antibodies. Pregnancies complicated with IUGR, decreased amniotic fluid, or hypertension were followed twice weekly by Doppler evaluation and fetal cardiotocography (CTG). All SLE pregnant patients received Prednisolone with dose ranging from 5 to 20 mg/day. Low dose Acetylsalicylic acid (81 mg) was described as soon as fetal pulsations were confirmed in the first trimester. Anticoagulation with low molecular weight heparin (LMWH) was used in all patients with APS and in patients with history of thrombotic events. Flares were treated with increased doses of Prednisolone up to 60 mg/day and/or introduction of medications as Hydroxychloroquine or Azathioprine.

Manifestations of SLE in pregnancy were identified and recorded. Pregnancy outcomes were assessed by occurrence of obstetric complications as abortion, intrauterine fetal death (IUFD), IUGR, development of preeclampsia (defined as new onset hypertension and proteinuria after 20 weeks' gestation), and preterm labor (before 37 weeks' gestation). Neonatal outcome was assessed by live births (term and preterm), LBW (less than 2.5 kg at birth), neonatal deaths (within 28 days after delivery), neonatal lupus syndrome or congenital heart block, and neonatal admission to intensive care unit (NICU).

The disease activity of SLE was evaluated using the SLE Disease Activity Index (SLEDAI). Active disease at conception was defined as SLEDAI score $\geqslant 2$ (12). SLE flare was defined as onset of new signs or worsening of disease during pregnancies in patients who are previously in remission. Flares included new or worsened cutaneous disease, arthritis, pleuritis, pericarditis, nephritis, hematological abnormalities as hemolytic anemia or platelet count below 60,000/μL, adding new drugs (Hydroxychloroquine and/or Azathioprine), hospitalization for SLE-related manifestations, increased prednisone dose, or increased SLEDAI score $\geqslant 3$.