



Original Article

# Pregnancy outcome of systemic lupus erythematosus in relation to lupus activity before and during pregnancy

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## Abstract

**Background:** To analyze the pregnancy complications and pregnancy outcome relating to the disease activity of systemic lupus erythematosus before conception and during pregnancy.

**Methods:** Seventy-two pregnancies were collected in a single tertiary medical center within a 5-year period. Twelve pregnancies were terminated due to various causes in the first half of pregnancy. Analysis of pregnancy complications and pregnancy outcome relating to the lupus activity before conception and during pregnancy was made among the remaining 60 pregnancies with gestational length > 26 weeks. The assessment of lupus activity was based on the routine monitoring, including urine routine, white blood cell count, hemoglobin and platelet count, erythrocyte sediment rate, serum titers of C<sub>3</sub>, C<sub>4</sub>, and double-stranded DNA. Monitoring of renal function with daily urinary protein loss and clearance rate of creatinine was needed when worsened nephropathy was suspected.

**Results:** The etiologies of the terminated pregnancies were deteriorated nephropathy (6 cases), involvement of central nervous system (1 case), unwanted pregnancy due to drug exposure (3 cases), and two early intrauterine fetal deaths (both during the 23<sup>rd</sup> week of gestation). Pregnancy complications were related to the lupus activity before conception [odds ratio = 0.238, 95% confidence interval (CI) = 0.073, 0.778,  $p = 0.014$ ] and during pregnancy (odds ratio = 0.153, 95% CI = 0.031, 0.754,  $p = 0.012$ ). Meanwhile, pregnancy outcome significantly related to the lupus activity of the preconception period and during pregnancy. The gestational length was significantly longer in the pregnancies with remitted lupus activity either before conception ( $38.2 \pm 1.6$  weeks vs.  $36.3 \pm 3.4$  weeks,  $p = 0.011$  and 95% CI =  $-3.454, -0.478$ ) or during pregnancy ( $38.2 \pm 1.6$  weeks vs.  $35.2 \pm 3.8$  weeks,  $p = 0.005$  and with 95% CI =  $-4.988, -1.005$ ). Significant relationships were also found between newborn birth weights and lupus activity preconceptionally ( $2940 \pm 389$  g vs.  $2448 \pm 674$  g,  $p = 0.002$  and 95% CI =  $-792, -192$ ) and after having conceived ( $2960 \pm 383$  g vs.  $2136 \pm 585$  g,  $p < 0.001$  and 95% CI =  $-1081, -568$ ). Multivariate analysis showed that lupus remission during pregnancy was correlated with a significantly longer gestation, since pregnant women with active lupus had a three-fold greater risk of preterm deliveries (hazard ratio = 3.022, 95% CI = 1.261, 7.242) compared with pregnant women without active lupus.

**Conclusion:** In order to reduce the incidence of pregnancy complication, especially preterm delivery, and to gain good pregnancy outcome, good preparation before conception and good control of the disease during pregnancy are mandatory.

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**Keywords:** nephropathy; pregnancy outcome; relapse; remission; systemic lupus erythematosus

Conflicts of interest: The authors declare that there are no conflicts of interest related to the subject matter or materials discussed in this article.

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## 1. Introduction

Systemic lupus erythematosus (SLE) is the most common immunologic disorder in women of reproductive age. It produces specific symptoms and signs of involved organs. Fertility is not affected when the disease activity is controlled.<sup>1</sup> Stable preconceptional lupus activity is recommended for planning pregnancy.<sup>2</sup> However, some patients become pregnant unexpectedly without remission. Termination of pregnancy may not be needed if there were neither severe lupus nephropathy nor involvement of central nervous system at the time of conception.

Many complications, such as abortion, fetal loss, preterm birth, pregnancy-induced hypertension, preeclampsia superimposed on chronic hypertension, intrauterine fetal distress, and fetal growth restriction make pregnancies with lupus very complicated, especially in those cases who were not well prepared for conception.<sup>3–5</sup> However, the correlation between pregnancy outcome and preconceptional lupus activity was still questionable for lack of convincing analysis. In this study, statistical analyses of the pregnancy complications and pregnancy outcomes associated with the lupus activity before conception and during pregnancy was done only on those cases that gave birth after completing 26 weeks of gestation.

## 2. Methods

From July 2008 to June 2013, all pregnant women suffering from SLE who gave birth to their babies in a single tertiary center hospital (Taipei Veterans General Hospital, Taipei, Taiwan) were enrolled in this study. With permits of the patients, the following data were collected: age, gravidity, parity, age at the onset of disease, duration of disease, lupus activity before and after conception, complications during pregnancy, newborn birth weight, gestational age at delivery, and medications given before conception and during pregnancy. All the women enrolled were followed-up regularly at the prenatal clinic and at least once per month by a rheumatologist. Intensive care was given when the disease activity was relapsing (flare-up) or becoming worse.

Other than clinical symptoms, the assessment of the lupus activity was based on the routine monitors, including urinalysis, white blood cell count, hemoglobin level, platelet count, erythrocyte sediment rate, and serum levels of C<sub>3</sub>, C<sub>4</sub>, and double-stranded DNA. Monitoring renal function with daily urinary protein loss and measurement of creatinine clearance as well as serum blood urea nitrogen and creatinine were needed, especially when exacerbated nephropathy was suspected. If the above measurements were all within normal limits, the patient's lupus activity was defined as "stable" or "in remission". Lupus activity was defined as "relapsed" or "without remission" when some or all of the above measurements went out of normal limits in those cases who were originally with remission. It was defined as "deteriorated" or "exacerbated" when some or all of the above measurements were worsening in those cases that were originally not remitted.

Pregnancy complications included threatened abortion, preterm labor, preterm delivery, gestational diabetes mellitus (GDM), pregnancy-induced hypertension, preeclampsia, chronic hypertension, intrauterine chronic fetal distress, intrauterine growth restriction (IUGR), and perinatal loss (including intrauterine fetal death and neonatal loss).

The data were analyzed with independent-sample *t* test between continuous variables, and with  $\chi^2$  test between noncontinuous variables. Survival (preterm delivery, defined as delivery occurring at < 37 weeks of gestation) was determined on the basis of parameters and patient outcomes. Estimates of the proportion of overall survival (OS) were calculated by the Kaplan–Meier procedure, and differences in survival were evaluated via log-rank test. Covariance analysis and the hierarchic  $\chi^2$  test were used to control for potential confounding factors in the comparison of patients' characteristics and risk factors. The log-rank test, hazard ratio (HR), and 95% confidence interval (CI) of preterm births from pregnant women with SLE were calculated via Cox proportional hazards model with univariate and multivariate analysis of OS. SPSS version 20 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Statistical significance was determined by unpaired two-tailed Student *t* test using a pooled estimator of variance, and was defined as  $p < 0.05$ . The study project was approved by the Institutional Review Board of Taipei Veterans General Hospital (IRB No. 2011-12-0171B#1).

## 3. Results

Sixty-five women with SLE had 72 pregnancies during the study period from July 2008 to June 2013. Twelve pregnancies in 12 patients were excluded due to termination for various causes in the first half of pregnancy. Six of them were terminated due to deteriorated lupus nephropathy. One of these six patients died thereafter due to poor response to immunosuppressive treatment. Of the remaining six pregnancies, one was terminated due to the involvement of the central nervous system by SLE; three were terminated because of drug exposure; and the remaining two were terminated due to intrauterine fetal death. One fetal death resulted from twisted cord found during the 23<sup>rd</sup> week of gestation, and the other one was the consequence of deteriorated nephropathy during the 23<sup>rd</sup> week of gestation.

The remaining 60 pregnancies in 55 women who gave birth to their newborns after 26 completed weeks' gestation were divided into two groups based on the preconceptional lupus activity, with remission and without remission. There were 34 (56.7%) cases with remission, and the remaining 26 (43.3%) cases were not remitted preconceptionally. The same work was done on the base of lupus activity during pregnancy. At delivery, the remission group had 43 cases and the remaining 17 cases were without remission. The total number of deliveries during the same period of time was 9419. The incidence of delivery with SLE was 0.64% (60/9419).

Mean age of the patients of the 60 pregnancies was  $29.7 \pm 4.8$  years old, with range between 20 years and 43

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