Decrease in Pregnancy Loss Rates in Patients with Systemic Lupus Erythematosus Over a 40-Year Period

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ABSTRACT. ***Objective.*** To determine if there has been a statistically significant change in pregnancy loss and preterm delivery rates in patients with systemic lupus erythematosus (SLE).

Methods. We analyzed the pregnancy outcomes of our SLE patients over the past 3 years and reviewed the literature over the past 40 years. We extracted pregnancy loss and preterm delivery data from reports of postdiagnosis SLE pregnancies. Studies were grouped into 5-year periods and weighted according to sample size. Group means, calculated for each study period, were plotted using linear regression to determine significance, and compared with population norms for the same periods.

Results. The rate of loss in SLE pregnancies over the past 40 years decreased from a mean of 43% in 1960–1965 to 17% in 2000–2003 ($r^2 = 0.648$). This approximates the pregnancy loss rate in the general US population. Preterm deliveries were not uniformly reported and were rarely stratified into spontaneous or physician-initiated. Prior to 1980, it was not possible to derive group means for each time period. From 1980 to 2002, however, there was a trend toward a decrease in preterm births in SLE pregnancies, although they continue to be more frequent in SLE than in the general population.

Conclusion. Improvements in disease management and perinatal monitoring have resulted in a significant decrease in pregnancy loss in SLE over the last 40 years and a trend toward decreased preterm deliveries over the last 20 years in comparison to the general population. These advances highlight the importance of collaboration between rheumatologists and perinatologists. Given these data, the description of SLE-associated pregnancy could be revised to reflect a more positive prognosis for mother and fetus. (J Rheumatol 2005;32:1709–12)

Key Indexing Terms:
SYSTEMIC LUPUS ERYTHEMATOSUS PREGNANCY LOSS
PRETERM DELIVERY RATES

Systemic lupus erythematosus (SLE) continues to be described as a condition associated with poor pregnancy outcome despite advances in disease management and perinatal care. We wanted to determine if there has been a statistically significant change in pregnancy loss and preterm delivery rates in women with SLE over the last 40 years in comparison with the general population.

MATERIALS AND METHODS

Patient selection. We reviewed the pregnancy outcomes (pregnancy loss, live birth, and preterm delivery) of our patients with SLE over the last 3 years. Preterm deliveries were defined as those spontaneously occurring at less than 37 weeks' gestation, in contrast to those precipitated by the physician as the result of deteriorating maternal or fetal well being.

Literature review. In a literature review using the US National Library of Medicine PubMed database, we extracted pregnancy loss (including both early and late losses) and preterm delivery data (whether specified as spontaneous or not) from literature published over the last 40 years for women diagnosed with SLE. Values for the total number of pregnancies, fetal loss rates, and preterm delivery rates were elicited from each study.

For comparison, 5-year grouped US population values for pregnancy losses from 1960 to 2000 and preterm births (defined as deliveries at < 37 weeks' gestation) from 1980 to 2000 were calculated from data provided by National Vital Statistics Reports[1,2].

Analysis. Data were analyzed using Sigma Stat version 4.0 (SPSS, Chicago, IL, USA). Mean values were calculated for 5-year periods from 1960 to 2003, and values were plotted using linear regression analysis (with 95% confidence intervals, CI) to determine the significance of any trends over time.

RESULTS

Pregnancy outcome in our clinic. Of 83 pregnancies in women with SLE attending our clinic over the last 3 years, 73 (83%) resulted in a live birth. Of the 73 deliveries, 50 had spontaneous onset of labor, 17 of which (34%) occurred prior to 37 weeks' gestation.

Literature review and analysis. We identified more than 35 studies published since 1963 with pregnancy loss data available for patients diagnosed with SLE[3-37].

Studies were collated into 5-year periods as some years had no available SLE pregnancy data. Because the sample mean is sensitive to a few unusually large or small observa-

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tions, we used a trimmed sample mean. Studies with results that differed significantly from other studies in the same 5-year time period (< 25th or > 75th percentile) were not included in the analysis. Results were weighted accordingly by combining raw data from studies grouped into the 5-year periods starting with 1963.

Change in fetal loss rate in SLE pregnancies. The rate of loss in SLE pregnancies decreased over the past 40 years from a mean of more than 40% to a mean of 17%. Despite interclinic variation within time periods, overall there has been a significant trend toward increased live birth rates (Figure 1; $r^2 = 0.648$). In comparison, pregnancy loss rates in the US have remained relatively stable since 1960: in 2000, it was reported that the pregnancy loss rate was 16.1%[1] (Figure 1).

Change in preterm delivery rates in SLE pregnancies. The definition of preterm delivery varied from ≤ 36 weeks to ≤ 38 weeks among available SLE studies from 1980 to 2002, and was not generally reported in the earlier literature. There was seldom any delineation between spontaneous or induced onset of preterm labor. We therefore analyzed data from individual studies (in contrast to grouped data) and found a trend toward a decrease in preterm delivery rate (< 37 weeks' gestation) from 1980 to 2000 (37.3% to 32%, respectively), but this was neither consistent nor statistically significant ($r^2 = 0.418$; Figure 2). In contrast, there has been a slight but significant increase in the percentage of preterm births in the US over the same period (from 9.4% in 1981 to 12.1% in 2002; $r^2 = 0.997$)[2].

DISCUSSION

Our review was hampered by inconsistent reporting and variable definitions of events in the SLE literature. The term "fetal loss" comprised losses at all stages of pregnancy (from embryonic to stillbirth), and in many instances, the term "preterm delivery" (defined as < 36 to < 38 weeks' gestation) was not stratified as spontaneous or induced. In addition, statistical analysis had to account for sample sizes that varied from 11 to 108. Our results must be interpreted in the context of these difficulties. Nevertheless, it is apparent that there has been a significant decline in pregnancy loss rates in SLE over the last 40 years compared to the relatively stable rate in the general population over the same time period.

There are a number of factors contributing to the decline in pregnancy loss (and potentially preterm births) among women with SLE from both the maternal and the fetal standpoint. Disease management, particularly the identification and treatment of secondary antiphospholipid syndrome (APS), may be the most significant clinical advance in the last 2 decades, although there is still debate regarding the optimum therapeutic regimen for women with a history of thrombosis and/or recurrent pregnancy loss. There is also recognition that inactive disease in contrast to stable disease is an important consideration in reducing both maternal and fetal morbidity[37].

In addition, as timing of delivery is a highly critical aspect of antenatal management, measures including fetal biometry, amniotic fluid volume, heart rate patterns, arterial and venous Doppler, and biophysical variables are now inte-

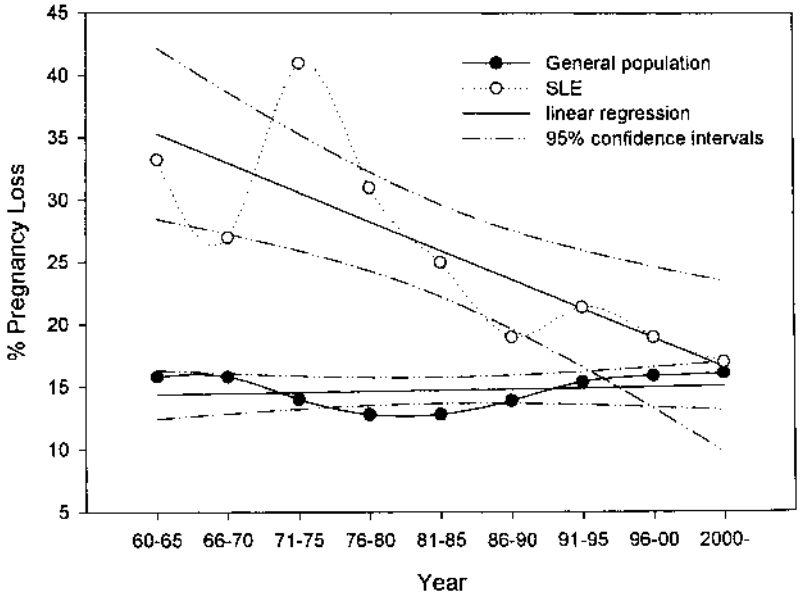

Figure 1. Change in rate of fetal loss in SLE pregnancies and in the US general population over that last 40 years. Data were grouped into 5-year periods (except the first period, 1963-65, and last period, 2001-2003).

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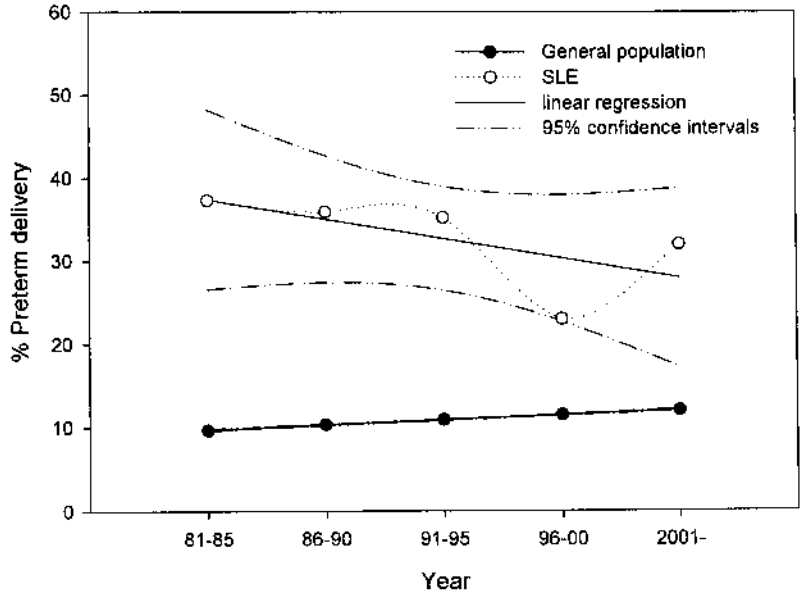

Figure 2. Change in rate of preterm deliveries (< 37 weeks' gestation, spontaneous and induced) in SLE pregnancies and in the US general population over the last 20 years.

gral parts of comprehensive fetal evaluation[38]. Clinicians are able to intervene and induce delivery in cases of deteriorating maternal or fetal health. Depending upon the gestational age, these induced deliveries might even be termed "fortuitous live births," as 20 years ago, no intervention would have been possible and the pregnancy would have terminated from either maternal or fetal causes with a resultant intrauterine death.

Kitridou and Goodwin[39] reviewed pregnancy outcomes in patients with SLE over the last half century and also reported rates approaching the population norm, but there was no mention of change in preterm deliveries. The increase in fetal survival due to improved pregnancy management was also raised by Petri and Allbritton[40], although the authors concluded (in 1993) that adverse pregnancy outcomes in lupus, including loss and preterm delivery, were still very common. In the intervening 12 years, that perception has gradually changed.

Pregnancy in women with SLE continues to be contraindicated in the context of severe organ disease or a history of life-threatening complications in previous pregnancies. For SLE patients without those superimposed conditions, however, there should be no contraindication for pregnancy, providing disease is clinically quiescent at the outset and there is appropriate planning and close prenatal monitoring.

We continue to advocate that SLE pregnancies be treated as high risk. However, based upon our review of the literature, we propose that the prevailing description of pregnancy in patients with SLE be revised to reflect advances in disease and perinatal management over the last 40 years.

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