Editorial

Pregnant Adolescents and Youth with Systemic Lupus Erythematosus: Can New Data Inform Our Approach to Young Women with SLE?

Pregnancy in women under the age of 20 years has been the norm for most of history. Changes that include increased control of reproduction through use of contraceptive methods and abortion, societal demand for education for girls, and increased length of education for all have led to increasing maternal age in developed countries over the past century. As the age of childbirth has gone up, teenage pregnancy has been increasingly identified as a problem associated with poverty, poor educational outcomes, single parenting, domestic violence, and other issues[1]. Adolescent pregnancy in healthy teens has been examined extensively in the United States; however, research on reproduction in adolescents with chronic conditions is sparse.

In this issue of *The Journal*, Silva and colleagues examine reproductive outcomes in Brazilian adolescents and young adults with juvenile systemic lupus erythematosus (JSLE)[2]. The authors point out that in studies of adults with SLE, the presence of active disease at any time during pregnancy is associated with a worse fetal prognosis and with increased rates of maternal diabetes, urinary tract infections, and pre-eclampsia. In addition, exposure to cyclophosphamide or methotrexate results in a high rate of fetal loss. Pregnancy loss in studies of adults with SLE has been reported to be between 15% and 30%. Similar data are not available for young females with JSLE.

The authors reviewed the charts of 449 female patients with JSLE for pregnancy data and outcome. These young women were patients at 12 Brazilian pediatric rheumatology centers. After excluding those under 10 years old at the time of the study, those who had not yet attained menarche, and those with amenorrhea not related to pregnancy, they were left with 315 young women between ages 10 and 22 years. Because data related to termination of pregnancies could not be extracted, they analyzed the data on young women who disclosed pregnancies to their healthcare providers; it is likely that some pregnancies were terminated and that the reported pregnancy rate is lower than the actual one. In addition, it is likely that some of these women had fetal loss at very early stages and thus they were not even aware that they were pregnant.

Their results showed pregnancy outcomes similar to those reported in adults. There were 28 pregnancies (a rate of 8%) in this group, 4 of which were excluded from analysis (3 were in their first trimester at time of study and one pregnancy occurred before SLE diagnosis). No maternal deaths, gestational diabetes, or premature rupture of membranes occurred. Ten patients were under age 18 years at the time of their due date and their rate of fetal loss was not statistically different from the 18- to 22-year-old adults. Predictably, the worst outcomes were in the pregnancies inadvertently exposed to cyclophosphamide during the first trimester.

There were 18 live births in this group of 24 pregnancies. Most losses were early in pregnancy. The only late loss was secondary to pre-eclampsia and premature birth at 34 weeks. Eleven percent of babies were premature and there was one neonatal death in a child with Down syndrome and severe cardiac malformations. Thirty-nine percent of live births were growth-retarded. The authors tell us that there is an extremely high rate of intrauterine growth restriction in Brazilian young women, so the high rate in this study cannot be attributed to maternal lupus[3].

Although the pregnancies that resulted in fetal loss were more likely to have active diffuse proliferative glomerulonephritis, proteinuria, arterial hypertension, and SLE Disease Activity Index-2K score ≥ 8, after logistic regression analysis only cyclophosphamide use remained as an independent risk factor for fetal loss. Use of prednisone, azathioprine, and plaquenil was the same in the groups with and without fetal loss. Frequency of positive anticardiolipin antibody and lupus anticoagulant were also similar in the 2 groups, although one case of fetal loss was associated with antiphospholipid antibody syndrome.

This group of young Brazilians with JSLE was very similar to healthy Brazilians in their age of menarche and sexual debut[4]. Young women in Brazil, whether healthy or with

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JSLE, are experiencing sexual debut at a similar age as in other countries[5].

What is to be learned from this study? We now know that women with JSLE under the age of 22 are as likely to experience fetal loss as adults with SLE. Therefore it appears that age is not a factor influencing pregnancy outcome. This seems counterintuitive, as one would expect that the older someone gets, the more likely they are to be sick, and to have a worse pregnancy outcome. However, adults are more likely to plan pregnancies and to therefore make an attempt to avoid times of poor health when getting pregnant, as well as seek early prenatal care. If adolescents with lupus were to plan their pregnancies, they might have better outcomes than adults.

The unfortunate loss of 3 fetuses (half the fetal loss in the study) because of inadvertent use of cyclophosphamide highlights the importance of attending to the reproductive status of young women in our care. Despite being advised to use contraception while taking cyclophosphamide, more than 1% of this sample became pregnant while receiving it. The importance of counseling these young women, making sure that they not only understand the need for excellent contraception but that they also have access to it, cannot be overstated. In addition, when starting cyclophosphamide or methotrexate they should be given emergency contraception to have available if needed; current recommendations are for 1.5 mg of levonorgestrel (Plan B) to be taken as soon as possible after unprotected intercourse[6]. Efficacy declines with the passage of time, but usage within 72 hours significantly decreases pregnancy.

Contraception and reproductive issues should be addressed with all female adolescents with JSLE. Although the pregnancies were all described as unplanned, it is unlikely that most of these young women were actively trying to prevent pregnancy. There are many things that are associated with teen pregnancy, including having an adult sexual partner[7], having a history of sexual abuse[8], illiteracy[9], and poverty. It has also been shown that young women who wish to prevent a pregnancy need both good contraceptive education and easy access to methods of contraception[10]. Contraceptive options may be more limited in some of these young women who are at increased risk of antiphospholipid antibody syndrome while taking estrogen-containing contraception[11]. With added concerns about decreased bone density on injectable progesterone[12] in this population, which is at risk because of steroid use, contraceptive counseling can be complicated, but even more important than in the general population.

Based on these data, there is no reason to recommend that young women with JSLE delay wanted pregnancies if they are relatively healthy. Presumably the longer one lives with SLE, the greater the chances of flare and serious complications. A young woman might miss her chance to have a healthy pregnancy if she waits until she is in her 20s or 30s and her health has deteriorated.

The authors wisely advise that young women should be supported in their reproductive choices. If they are motivated to delay or prevent pregnancy, they should be given the information and access to contraception that will allow them to meet this goal. If they desire a pregnancy, they should be supported in embarking on this when they are in the best possible state to have a healthy outcome — that is, with their lupus under good control, taking folic acid, and refraining from alcohol and other such substances.

Silva, *et al* have made an important contribution to the literature on reproductive outcomes in adolescents with chronic conditions. We can only hope that their example will inspire other investigators to examine reproductive choices and outcomes in adolescents with other childhood-onset conditions.

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