Miscarriages, Terminations Rise After RA Onset

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SAN FRANCISCO — Women who got pregnant after the onset of rheumatoid arthritis had a slightly higher risk of miscarriage, compared with pregnant women as a whole, according to a study of 1,461 pregnancies in 636 women with rheumatoid arthritis.

Many more pregnancies in the retrospective study occurred before rheumatoid arthritis symptoms appeared than occurred after disease onset.

The 2% rate of pregnancy termination in the 86% of women who got pregnant before the onset of rheumatoid arthritis symptoms was significantly lower than a 6% termination rate among the 14% of women who got pregnant after developing arthritis, Dr. Cecilia Friden and her associates reported at the annual meeting of the American College of Rheumatology.

The investigators compared data on pregnancy histories in women who were enrolled in a hospital-based rheumatoid arthritis registry in Boston with U.S. data on pregnant women of comparable ages (20-44 years), and compared outcomes between women who became pregnant before or after developing arthritis.

The cohort's history of 1,461 pregnancies included 1,146 live births, with birth defects in 2% of neonates.

There was no association between the risk of birth defects and the timing of the onset of rheumatoid arthritis, said Dr. Friden of the Karolinska Institute, Stockholm.

The study did not collect information on the use of disease-modifying antirheumatic drugs.

Although the effects of pregnancy on rheumatoid arthritis (disease activity decreases during pregnancy and increases during the postpartum period and with breast-feeding) are well known, little has been known about the effects of rheumatoid arthritis on pregnancy outcomes, she noted.

More research will be needed to be able to correctly inform women with rheumatoid arthritis about the potential risks of pregnancy with the disease, Dr. Friden added.

Compared with the nationwide data on pregnant women, the investigators found that the women who had rheumatoid arthritis had slightly higher rates of miscarriage but slightly lower rates of stillbirths.

Pregnancy outcomes did not differ significantly between the pre- and post-arthritis pregnancy groups except for the termination rate.

The rate of miscarriages, stillbirths, multiple births, low-birth-weight babies, and infants born before or after 32 weeks did not differ significantly between the two arthritis groups.

Dr. Friden stated that she had no relevant conflicts of interest to report.

Her associates in the study have received research funds from pharmaceutical companies (some of which make arthritis medications) including Amgen Inc., Biogen Idec Inc., Bristol-Myers Squibb Co., and Millennium Pharmaceuticals Inc.

One associate has been a consultant for GlaxoSmithKline. ■

Rheumatoid Arthritis and Pregnancy Outcomes

	U.S. pregnancies	Pre-RA pregnancies	Post-RA pregnancies
Miscarriage	10%-15%	16%	20%
Stillbirth	2%	1%	0%
Birth weight under 2.5 kg	8%	6%	9%
Multiple births	3%	1%	3%

Note: Data on U.S. pregnancies are for all U.S. women of the same ages as those in the study (22-40 years). Pre- and post-RA categories represent 1,461 pregnancies in a Boston cohort that occurred before or after RA symptom onset.

Source: Dr. Friden

ELSEVIER GLOBAL MEDICAL NEWS

Reports on Birth Outcomes in Autoimmune Diseases From the ACR Meeting

Several posters at the annual meeting of the American College of Rheumatology reported on the following pregnancy outcomes for women who had autoimmune diseases or were taking drugs for autoimmune diseases:

► **Lupus.** A study of 198 women with clinically stable or mildly active systemic lupus erythematosus (SLE) at the time of conception found that they rarely developed severe SLE flares and generally had good pregnancy outcomes, Dr. Jane E. Salmon of the Hospital for Special Surgery, New York, and her associates reported.

Mild or moderate disease flares occurred in 6% of women within 20 weeks of gestation, in 5% at 32 weeks, and in 8% during the postpartum period, according to data from the PROMISSE (Predictors of Pregnancy Outcome: Biomarkers in Antiphospholipid Antibody Syndrome and Systemic Lupus Erythematosus) study.

No severe flares occurred by 20 weeks. Severe flares were seen in fewer than 1% of women by 32 weeks and in 1.5% during the postpartum period in the ongoing prospective, multicenter, observational study.

Of the four severe SLE flares, two involved the central nervous system, one involved kidney disease, and the other was an arthritis flare.

Pregnancy complications occurred in 15% of women, and included fetal death (in 8%), neonatal death (3%), preeclampsia (15%), and fetal growth restriction (10%), with some women having more than one complication.

Although 28% of women had a past history of renal disease and 39% had blood abnormalities associated with active lupus, these were not associated with flares or poor pregnancy outcomes, Dr. Salmon reported. The investigators reported no relevant conflicts of interest.

► **Etanercept.** Babies born to 139 women who took etanercept for autoimmune diseases during the first trimester of pregnancy had more than twice the rate of congenital anomalies, compared with the newborns of 67 women with the same diseases who were not on etanercept. The data came from the ongoing Autoimmune Diseases in Pregnancy Project run by OTIS (Organization of Teratology Information Specialists), a network of telephone-based teratogen counseling services in North American universities and hospitals. The project recruits women in a prospective cohort; the women are interviewed three times during pregnancy and their medical records studied. Pediatric specialists examine all live-born infants and follow them for up to a year.

In the etanercept group, major defects were seen in 9.4% of all pregnancies in the etanercept group and in 4.5% of the control group. Pregnancies resulted in live births in 94% of the etanercept group and 88% of the control group (due to a higher rate of spontaneous abortion in the control group).

Among live births, 8.5% in the etanercept group had major defects, compared with 1.7% of the control group, reported Dr. Diana L. Johnson of the University of California, San Diego, and her associates.

The two groups did not differ significantly in mean birth weight of full-term infants, mean gestational age at delivery of live births, or pregnancy terminations.

The women took etanercept to treat rheumatoid arthritis; psoriasis or psoriatic arthritis; ankylosing spondylitis; or multiple diseases.

The project is sponsored in part by grants from 10 pharmaceutical companies including Amgen Inc., which markets etanercept with Wyeth Pharmaceuticals.

► **Adalimumab.** The OTIS Autoimmune Diseases in Pregnancy Project also followed 33 women who took adalimumab for rheumatoid arthritis during the first trimester of pregnancy and followed them in the same manner as the etanercept cohort. Their birth outcomes were compared with birth outcomes of 52 pregnant women with the same disease but no adalimumab treatment and 45 pregnant women without rheumatoid arthritis.

Preliminary data from the ongoing study suggest that rates of spontaneous abortion, stillbirth, congenital defects, and preterm deliveries are similar between groups and within the expected range in the general population, Dr. Johnson and her associates reported in a separate poster. A larger sample size is needed, however, to draw firm conclusions, she added.

The companies that fund the project include Abbott Laboratories, which markets adalimumab.

► **Systemic sclerosis.** Worsening of systemic sclerosis and progression to organ problems in three out of five Hungarian women after pregnancy surprised investigators in a separate study. Previous reports identified a higher risk for maternal scleroderma renal crisis in the third trimester, but other than that have suggested that disease symptoms generally do not change or may improve during pregnancy.

The five pregnancies among 400 women with systemic sclerosis who were seen at two medical centers from 1995 to 2007 resulted in five infants with no severe organ complications, reported Dr. G. Szucs of the University of Debrecen (Hungary), and associates.

One mother with limited cutaneous disease had a normal, full-term delivery. One with diffuse cutaneous disease had a spontaneous preterm birth. Three women (one with limited cutaneous disease and two with diffuse systemic sclerosis) were delivered by C-section because of maternal hypertension and proteinuria with a high risk for renal crisis.

The hypertension and proteinuria disappeared after C-section delivery in one woman with diffuse disease, who was treated with an ACE inhibitor to avert renal crisis.

Three other women (one with limited disease and two with diffuse disease) developed severe manifestations of systemic sclerosis after delivery—fibrosing alveolitis; cardiomyopathy with arrhythmias or cardiac failure; renal failure; and/or rapidly progressing skin symptoms.

Pregnant women with systemic sclerosis "should be monitored often and carefully after delivery for not only renal but other life-threatening complications," Dr. Szucs suggested.