Increased Risk of Intrahepatic Cholestasis of Pregnancy in Women with Systemic Lupus Erythematosus Exposed to Azathioprine

Selected for Podium Presentation and Winner of Best Abstract by a Post-Graduate Research Trainee Award

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At the 2026 Canadian Rheumatology Association (CRA) Annual Scientific Meeting (ASM) in Halifax, Dr Reem Farhat, MD, PhD, a student in the Graduate Program in Clinical and Translational Research at McGill University, presented new findings that may reshape monitoring strategies for pregnant women with systemic lupus erythematosus (SLE) receiving azathioprine. Conducted under the supervision of Dr. Evelyne Vinet, MD, PhD, Associate Professor at the McGill University Health Centre, the study identified a markedly increased risk of intrahepatic cholestasis of pregnancy among SLE patients exposed to azathioprine.

Pregnancy in women with SLE is already recognized as high risk because of increased maternal and fetal complications. Azathioprine, a thiopurine drug, is the immunosuppressive of choice in SLE pregnancies. However, emerging signals from inflammatory bowel disease cohorts and a recent United States Food and Drug Administration safety report have raised concerns regarding a possible association between thiopurines and intrahepatic cholestasis of pregnancy, a pregnancy-specific liver disorder associated with preterm birth and stillbirth.

To better understand this risk in SLE pregnancies, investigators analyzed data from the Lupus in prEGnAnCY (LEGACY) cohort, an international prospective multicentre study conducted across Systemic Lupus International Collaborating Clinics in Canada, South Korea, Peru, and Mexico. Pregnant women with SLE were enrolled before 17 weeks gestation and followed throughout pregnancy. Since intrahepatic cholestasis of pregnancy generally develops after 20 weeks gestation, analyses were restricted to pregnancies with at least one second trimester visit.

The investigators observed more than a 10-fold increased risk of intrahepatic cholestasis of pregnancy among women exposed to azathioprine. In a subgroup with available thiopurine metabolite data, all patients with intrahepatic cholestasis of pregnancy demonstrated second trimester metabolite shunting, characterized by preferential production of the hepatotoxic metabolite 6-methylmercaptopurine. Half of the patients exhibiting this shunting pattern subsequently developed intrahepatic cholestasis of pregnancy. Azathioprine-exposed patients also appeared to experience more severe disease, including earlier delivery, lower birth weight for gestational age, and higher bile acid levels.

This research impacts rheumatology care by supporting heightened vigilance for intrahepatic cholestasis of pregnancy in pregnant patients with SLE receiving azathioprine, while highlighting a potential role for thiopurine metabolite monitoring to help identify those at increased risk. The goal is to improve maternal and fetal outcomes while maintaining access to an important therapy.

You are invited to submit abstracts for presentation during the **2027 CRA Annual Scientific Meeting!**
Deadline for submissions is **Friday, November 20, 2026**.
Details will be available at *asm.rheum.ca*.