Top Six Things Rheumatologists Should (And Might Not) Know About Pregnancy and Rheumatic Diseases

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The 10th International Conference on Reproduction, Pregnancy and Rheumatic Diseases was held in Bern, Switzerland from Sept 27-29, 2018, and attended by several Canadian rheumatologists. We, of course, missed Carl Laskin, who has inspired so many of us! Key learnings include the following:

1. Contraception

It is well known that low disease activity prior to conception results in better pregnancy outcomes, both for mom and baby. Unfortunately, 40-50% of pregnancies are unplanned. With the shortage of primary health care in Canada, the discussion surrounding contraception often falls to the rheumatologist. The Canadian Contraception Consensus[1] is a current and thorough resource to help guide discussion with patients, particularly those without access to primary care.

2. Fertility

Subfertility is reported in up to 48% of women with rheumatoid arthritis (RA); twenty-eight per cent (28%) of which is due to anovulation and 48% being unexplained. Higher maternal age, medication use (such as non-steroidal anti-inflammatory drugs [NSAIDs]) inhibiting ovulation, and low health-related quality of life (HRQoL) all contribute. Infertility treatment (IVF) is a safe option for women with connective tissue disease (CTD).

3. Pre-pregnancy Counselling

A key question we should be asking regularly to all women of childbearing age is "Would you like to become pregnant in the next year?" Pregnancy preparation in our patients is important and often begins months prior to conception. Start with a realistic risk assessment, stop harmful medications, use pregnancy compatible medications prior to conception, and reassure the patient. A risk assessment should include: previous pregnancy complications (preeclampsia), organ damage, recent/current disease activity, antibody status (lupus anti-coagulant [LAC], anti-cardiolipin [aCL], beta-2 glycoprotein 1 [2GPI], Ro/La), exposure to fetotoxic drugs, smoking and other chronic medical conditions.

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4. Pregnancy Compatible Medications

"Safe treatment in pregnancy" should be understood as "no evidence of risk," and as the safest option among eligible drugs and compared to the risk of untreated disease. Refer to the EULAR Points to Consider,[2] BSR Guidelines[3] and RheumInfo Pregnancy and Lactation brochure.[4] Prednisone use in any trimester is an independent risk factor for preterm birth. Higher doses are associated with shorter gestational length. Medication use in lactation is poorly studied: LactMed[5], a National Institute of Health (NIH) database, is updated monthly, and reports drug levels in milk, the infant, and possible adverse effects to the infant.

5. Peripartum Monitoring

Active CTD can be associated with defective placentation which leads to placental insufficiency, preeclampsia, intrauterine growth restriction (IUGR), and HELLP syndrome. Monitoring during pregnancy may include the following:

a. Screening for Ro/La antibodies. Risk of congenital heart block (CHB) is 1-2% overall and 10-20% in those with previous CHB. It develops between 18-24 weeks gestation and can be monitored by fetal echo. Hydroxychloroquine (HCQ) reduces risk by 50%. Once developed, the only proven treatment is a pacemaker.

b. Doppler screening for fetal growth restriction.

c. New markers for preeclampsia → (placental growth factor [PLGF]), soluble fms-like tyrosine kinase-1 (sFlt1)/PLGF ratio.

6. Pregnancy Behavior with Various Rheumatic Diseases:

a. Inflammatory arthritis (IA): Patients with stable IA generally have good outcomes. In RA, 29% flare during pregnancy, with higher risk in the third trimester and postpartum. SpA patients have higher risk of flare in the second trimester, whereas patients with juvenile idiopathic arthritis (JIA) tend to flare in the first few months postpartum. The risk of flare is higher when there is active disease at conception and when TNF inhibitors are discontinued.

b. Systemic lupus erythematosus (SLE): SLE in pregnancy mimics SLE prior to pregnancy: Prior to pregnancy you would want to see quiet nephritis, stable x 6 months, proteinuria < 1 gram/day, and no active sediment. Flare risk is low (< 3%) with inactive or stable active disease at conception and flare is reduced by 50% with HCQ, which should be continued through pregnancy. Helpful resources include RheumInfo[4] and the Healthy Outcomes in Pregnancy Hop-Step Program.[5]

c. Obstetric Antiphospholipid Syndrome (OAPS): OAPS is characterized by defective placentation (not placental infarction as previously thought). Beta-2-glycoprotein (ß2GPI) plays a pivotal role in the pathophysiology of OAPS and has potential as a screening tool. Seronegative OAPS has also been described. The soon to be published "Management of Maternal Antiphospholipid Syndrome"[7] includes treatment options according to clinical features. Maternal follow-up is recommended, as 20-60% of women with OAPS will eventually develop thrombosis (vascular APS).

d. Systemic sclerosis (SSc): Pregnancy has minimal impact on disease activity of patients with SSc. However, SSc is associated with higher risk of maternal (gestational hypertension, preeclampsia) and fetal (miscarriage, stillbirth, IUGR, preterm birth) complications. Severe pulmonary arterial hypertension (> 25mm Hg) is an absolute contraindication.

e. Takayasu Arteritis (TA): TA is associated with increased risk of gestational hypertension and preeclampsia. Patients with severe aortic valvular disease, aortic aneurysms and dissections have increased morbidity and mortality and should be counselled to avoid pregnancy.

f. Behcet's Disease: Patients with Behcet's Disease have no apparent increase in maternal, obstetrical or fetal complications during pregnancy. (See 2018 update of EULAR recommendations for Behcet's)[8]

The Canadian Pregnancy and Rheumatic Diseases Consortium* is a national database for the prospective observational study of pregnant patients with rheumatic disease, with sites at many academic centers across Canada.

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References available online at *www.craj.ca.*

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