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REVIEW

Pregnancy in women with autoimmune inflammatory rheumatic diseases: from pre-conception to post-partum care

RAZVAN ADRIAN IONESCU[1,2)]

[1)] *Colentina Clinical Hospital, 3rd Internal Medicine Department*
[2)] *UMF "Carol Davila", Internal Medicine Departament*

Abstract

Autoimmune inflammatory rheumatic diseases (AIRDs) — including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), psoriatic arthritis, ankylosing spondylitis, and systemic vasculitides — disproportionately affect women during their reproductive years.[1] Historically, pregnancy in these patients was associated with significant maternal and fetal morbidity. However, advances in pharmacologic management, the development of evidence-based guidelines by European Alliance of Associations for Rheumatology (EULAR), American College of Rheumatology (ACR), and British Society for Rheumatology (BSR), and the adoption of multidisciplinary care models have substantially improved outcomes[1]. This review synthesizes current evidence across four phases: pre-pregnancy optimization, pregnancy management, multidisciplinary care models, and post-partum considerations, with emphasis on shared decision-making and individualized treatment strategies.

Keywords:. autoimmune inflammatory rheumatic diseases; pregnancy; preconception care; disease activity; biologic DMARDs.

Pre-pregnancy phase: optimizing outcomes before conception

Reproductive counseling as a core element of rheumatology care

Since some of the most important rheumatological disease are inflammatory in nature and affect women of reproductive age, structured reproductive life-planning is now recognized as an integral component of rheumatology practice. The ACR 2020 guideline recommends that rheumatologists treating reproductive-age women discuss contraception and pregnancy plans at an initial or early visit and periodically thereafter, and always when initiating treatment with potentially teratogenic medications[1]. The "One Key Question" approach — "Would you like to become pregnant in the next year?" — has been proposed as a simple screening tool to initiate family planning discussions[1].

A lot of pregnancies are unplanned and, in women with AIRDs, unplanned pregnancies carry substantially greater risk than those planned, that is those conceived during periods of low disease activity on compatible medications[1]. That is because an active AIRD may have deleterious consequences both on the mother and the embrio/foetus. Effective contraception should therefore be discussed and encouraged, with attention to both efficacy and safety. Long-acting reversible contraceptives (LARCs) are generally preferred for their high efficacy, while estrogen-containing methods require caution in patients with primary or secondary antiphospholipid syndorme (APS) or antibodies (aPL), due to the potential thrombotic risk incumbed by the presence of these antibodies[1].

Shared decision-making models are essential in this context. Patient education tools and decision aids can help women understand the interplay between disease activity, medication safety, and pregnancy outcomes, empowering them to participate actively in reproductive planning[1]. Periconceptional counseling should address the timing of pregnancy relative to disease activity, the need for medication adjustments, fertility preservation options (particularly before cyclophosphamide therapy), and the importance of sustained remission before conception[1].

Disease activity control prior to conception

The impact of disease activity at conception on pregnancy outcomes is well established. Active disease at the time of conception is the strongest independent predictor of disease flare during pregnancy and the post-partum period, and is associated with increased rates of preeclampsia, preterm birth, fetal growth restriction (FGR), and pregnancy loss[1,2]. In SLE, achieving remission or

low disease activity for at least several months on pregnancy-compatible medications prior to conception is essential; with close management and well-controlled disease, fewer than 10% of patients experience flares during pregnancy[1].

Treat-to-target strategies should be adapted for women planning pregnancy. The goal is to achieve sustained remission or the lowest possible disease activity using medications that are compatible with pregnancy, before conception is attempted[1]. When potentially teratogenic medications are discontinued, there are strong recommendations for a period of observation — typically a minimum of several months — to ensure disease stability on the new regimen before attempting conception[1].

The risks of treatment discontinuation must be carefully weighed. Abrupt cessation of effective therapy may precipitate disease flares that are themselves harmful to both mother and fetus. In RA, for example, Mendelian randomization analyses have demonstrated a genetic association between RA and increased odds of preterm labor (OR 1.03, 95% CI 1.01–1.06), preeclampsia (OR 1.04, 95% CI 1.01–1.07), and poor fetal growth (OR 1.08, 95% CI 1.04–1.12) [3]. These findings underscore the importance of maintaining disease control rather than simply eliminating all pharmacotherapy.

Pharmacologic management in women of childbearing age

The safety profiles of antirheumatic drugs in the context of pregnancy have been extensively evaluated by EULAR (2016 and 2024 updates), ACR (2020), and BSR, with broadly concordant recommendations for conventional synthetic DMARDs (csDMARDs) and some divergence regarding biologic DMARDs (bDMARDs) and targeted synthetic DMARDs (tsDMARDs) [1,4].

Medications considered compatible with pregnancy include hydroxychloroquine (HCQ), azathioprine, sulfasalazine, colchicine, cyclosporine, and tacrolimus[1]. HCQ is particularly important in SLE, where its continuation during pregnancy is strongly recommended by both ACR and EULAR, as discontinuation is associated with increased flare risk[1].

Known teratogens — methotrexate (MTX), mycophenolate mofetil (MMF), cyclophosphamide (CYC), and thalidomide — must be discontinued at least 3 months prior to conception[1]. For leflunomide, cholestyramine washout is strongly recommended if serum metabolite levels are detectable, given the drug's prolonged half-life due to enterohepatic circulation[1].

Regarding bDMARDs, tumor necrosis factor inhibitors (TNFi) have the most robust safety data. Certolizumab pegol, which lacks an Fc fragment and therefore has minimal placental transfer, is strongly recommended for continuation throughout pregnancy[1]. Other TNFi (infliximab, etanercept, adalimumab, golimumab) are conditionally recommended for use during pregnancy, with the option of discontinuation in the third trimester if disease is well controlled[1]. The 2024 EULAR update further supports that all TNFi can be used throughout pregnancy based on individualized risk-benefit assessment, and that non-TNFi bDMARDs may be used if needed[1].

Non-TNFi biologics (anakinra, abatacept, tocilizumab, belimumab, secukinumab, ustekinumab) have more limited pregnancy safety data. The ACR conditionally recommends continuing these agents while trying to conceive but discontinuing upon confirmation of pregnancy[1]. Rituximab may be continued during pregnancy only for severe, life- or organ-threatening disease[1].

For tsDMARDs (tofacitinib, baricitinib, upadacitinib, apremilast), pregnancy safety data remain insufficient, and these agents are generally not recommended during pregnancy[1,4]. A scoping review of 18 international guidelines found significant variability in recommendations for bDMARD and tsDMARD use, reflecting the limited evidence base[4].

NSAIDs are conditionally compatible with pregnancy in the first two trimesters but are strongly contraindicated in the third trimester due to the risk of premature closure of the ductus arteriosus[1]. Glucocorticoids should be used at the lowest effective dose; it is recommended to taper prednisone to less than 20 mg daily and adding pregnancy-compatible steroid-sparing agents when needed [1].

Pregnancy phase: balancing maternal and fetal health

Disease management during pregnancy

Maternal disease activity during pregnancy is a strong predictor of adverse obstetric outcomes. In SLE, physician-assessed disease activity is associated with preterm birth (OR 2.9, 95% CI 1.3–6.3), cesarean delivery (OR 2.3, 95% CI 1.0–5.3), and preeclampsia (OR 2.8, 95% CI 1.3–6.3) [4]. In RA, both patient-reported and physician-reported disease activity predict preterm birth and small-for-gestational-age infants[4].

Flare prevention strategies during pregnancy center on maintaining effective therapy. All patients with SLE should continue HCQ throughout pregnancy[1]. Low-dose aspirin is recommended starting in the first trimester to reduce preeclampsia risk[1,5]. For patients with antiphospholipid syndrome (APS), combination prophylactic heparin/low-molecular-weight heparin (LMWH) plus low-dose aspirin is strongly recommended[1].

The use of biologics across trimesters requires consideration of placental transfer kinetics. Most IgG1-based bDMARDs do not cross the placenta in significant concentrations until the second trimester, as active transport via the neonatal Fc receptor (FcRn) increases progressively[1,4]. Third-trimester use of Fc-containing TNFi results in high neonatal drug levels, though no clear adverse effects have been

demonstrated[1,4]. Certolizumab, lacking an Fc fragment, has minimal placental transfer and can be continued throughout pregnancy without concern for fetal exposure[1].

Meta-analyses with adjusted risk estimates have not revealed adverse pregnancy outcomes or serious infant infections to be associated with TNFi use[2]. Data on non-TNFi bDMARDs have similarly not raised major concerns, though evidence remains more limited[1,2]. Regarding glucocorticoids, a dose-dependent association with increased risk of preterm birth has been identified[2].

Pregnancy complications in rheumatic diseases

Women with AIRDs face elevated risks of multiple obstetric complications. In SLE, preeclampsia occurs in approximately 15–35% of pregnancies, preterm birth rates range from 19% to 49%, and FGR affects 6–35% of pregnancies[5]. SLE with APS is associated with a 3-fold increased risk of pregnancy loss[5]. Placentas in SLE pregnancies are typically smaller and frequently exhibit vascular lesions including decidual vasculopathy, thrombosis, and infarction[5].

Women with anti-Ro/SSA or anti-La/SSB antibodies require additional fetal monitoring, as their offspring are at increased risk for congenital heart block[1]. Serial fetal echocardiography is recommended in these cases. Distinguishing lupus nephritis flare from preeclampsia during pregnancy is particularly challenging, as both may present with proteinuria, hypertension, and renal dysfunction; HELLP syndrome may further complicate the differential diagnosis[1,2].

Antenatal surveillance should include serial growth scans and fetal testing, typically initiated by 32 weeks of gestation, with earlier and more frequent monitoring individualized for patients with complicated disease[5]. Timing and mode of delivery should be individualized based on disease activity, complications, and comorbidities [5].

Shared decision-making in high-risk pregnancy

Communicating uncertainty and risk during pregnancy is a critical skill for the multidisciplinary team. The evidence base for many pregnancy management decisions in AIRDs derives from observational studies and case series rather than randomized controlled trials, and many recommendations are therefore conditional[1,2].

Patient-reported outcomes (PROs) may serve as useful adjuncts to physician assessments. In RA, patient-reported disease activity measures are associated with adverse pregnancy outcomes and may help identify pregnancies at greater risk[4]. In SLE, however, PROs have not shown the same predictive value, highlighting the importance of physician-assessed disease activity indices such as SLEDAI[4,5].

Incorporating patient values into treatment adjustments is essential. Many patients are hesitant to use antirheumatic medications during pregnancy, and honest, accurate discussions about the risks of untreated disease versus medication exposure are critical to informed decision-making [1,4].

Multidisciplinary and personalized care models

Multidisciplinary Team (MDT) care in pregnant patients

The complexity of pregnancy in women with AIRDs necessitates coordinated care among rheumatologists, obstetricians or maternal-fetal medicine (MFM) specialists, and, when appropriate, nephrologists, hematologists, and neonatologists[1,2,5]. Usually, obstetrics-gynecology or MFM specialists necessarily assume primary medical management of pregnancy, while rheumatologists play a critical role in disease monitoring, medication management, and distinguishing disease flares from pregnancy-related complications[2].

Pregnancy-related physiologic changes — including increased intravascular volume, elevated glomerular filtration rate, hypercoagulability, and symptoms such as malar erythema, anemia, and arthralgias — may mimic or mask active rheumatic disease[2]. Pregnancy-induced hypertensive syndromes may be confused with lupus nephritis, scleroderma renal crisis, or vasculitis flare. Distinguishing among these syndromes requires the combined expertise of rheumatologists and obstetric providers[2].

Care pathways for high-risk pregnancies should include preconception risk stratification, regular multidisciplinary review during pregnancy, standardized monitoring protocols (including laboratory assessments at least once per trimester in SLE), and coordinated delivery planning[1,5]. Ienterdisciplinary care starting from the pre-pregnancy period and extending through pregnancy and breastfeeding has been shown to improve both fetal and maternal outcomes [1].

Post-partum phase: after delivery and beyond

Post-partum disease flares and long-term control

The post-partum period represents a high-risk window for disease flare in women with AIRDs. A retrospective analysis of 253 pregnancies in women with systemic autoimmune diseases found that post-partum complications occurred in 19.8% of patients, with disease flares accounting for 16.6% of cases[4]. Inflammatory arthritis showed the highest flare rate (41.7% vs. 12.0% in connective tissue diseases), though severe flares occurred predominantly in connective tissue diseases and vasculitis[4]. Flares

were significantly associated with active disease during pregnancy[4].

In RA, pregnancy improves symptoms in approximately 75% of patients, but relapse occurs within six months post-partum in up to 90% of cases[6]. In SLE, the incidence of flare is increased during pregnancy and within the 3 months post-partum, with a hazard ratio of 1.59 (95% CI 1.27–1.96) compared with non-pregnant periods[4]. Importantly, HCQ use mitigates this risk: the HR for flare was 1.83 (95% CI 1.34–2.45) without HCQ versus 1.26 (95% CI 0.88–1.69) with HCQ[4].

Timing of treatment re-initiation after delivery is critical. Prophylactic medication changes are not routinely recommended, but patients should be informed of the potential for worsening symptoms and evaluated more frequently, as needed[5]. Delayed treatment re-initiation may lead to sustained disease activity and cumulative organ damage. Patients who required lifelong anticoagulation can be transitioned back to anti vitamin K anticoagulants after delivery, while those with obstetric APS are generally continued on LMWH for 6 weeks post-partum [1,5].

Breastfeeding and medication safety

Breastfeeding should be encouraged in women with AIRDs, and disease control should be maintained with lactation-compatible medications[1]. The ACR, EULAR, and BSR guidelines are broadly concordant in their recommendations[1].

Medications strongly recommended as compatible with breastfeeding include HCQ, colchicine, sulfasalazine, all TNF inhibitors, and rituximab[1]. Conditionally compatible medications include azathioprine, calcineurin inhibitors (cyclosporine, tacrolimus), NSAIDs, and non-TNFi biologics (anakinra, belimumab, abatacept, tocilizumab, secukinumab, ustekinumab)[1]. The 2024 EULAR update considers all bDMARDs compatible with breastfeeding[1].

Prednisone at doses below 20 mg daily is compatible with breastfeeding. At doses ≥20 mg daily, women should delay breastfeeding or discard breast milk accumulated in the 4 hours following glucocorticoid administration[1]. Cyclophosphamide, leflunomide, MMF, and thalidomide are strongly contraindicated during breastfeeding. Methotrexate is conditionally recommended against, as it may accumulate in neonatal tissues despite minimal passage into breast milk[1].

Drug levels in breast milk are expressed as the relative infant dose (infant dose mg/kg/day divided by maternal dose mg/kg/day); a value below 10% is generally considered safe[1]. Rheumatologists should collaborate with pediatricians when making breastfeeding recommendations, particularly for premature infants or those with gastrointestinal disorders who may absorb medications differently [1].

Neonatal considerations

Infants born to mothers with AIRDs require specific monitoring and vaccination considerations. Non-live (inactivated) vaccines should be administered according to national schedules and have been shown to be both safe and effective in infants exposed to bDMARDs in utero[5,7].

For live-attenuated vaccines, recommendations vary by guideline and by specific biologic exposure. The BCG vaccine should be delayed for at least 6 months in infants exposed to TNFi in utero, as several fatal cases of disseminated tuberculosis have been reported following BCG administration in TNFi-exposed infants[2,7]. Regarding rotavirus vaccination, the ACR 2022 guideline conditionally recommends that rotavirus vaccine can be given to infants exposed to TNFi in utero, while the AAP recommends delaying rotavirus vaccination for 12 months after in utero exposure to bDMARDs other than certolizumab (due to its very low materno-fetal passage) [4]. Observational studies of 58 children exposed to bDMARDs who received live rotavirus vaccines reported no clear adverse events[4]. EULAR recommends delaying live vaccines for 6 months in infants exposed to bDMARDs later in pregnancy, with the caveat that measurement of serum drug concentrations in infants could guide decision-making[5].

For infants exposed to rituximab in utero during the second or third trimester, B lymphocyte levels may be low or absent at birth, with recovery typically occurring within 6 months[4]. Vaccination responses may be impaired during this period, and rotavirus vaccination should be delayed until after 6 months of age[4,5].

Monitoring of neonates born to mothers with autoimmune disease should also include assessment for neonatal lupus syndrome in infants of mothers with anti-Ro/SSA or anti-La/SSB antibodies, with particular attention to congenital heart block, which may occur in 1–2% of exposed pregnancies[1]. After delivery, pediatricians should be informed of all maternal medications used during pregnancy, as they may not be aware of the impact of in utero medication exposure on vaccine safety and immunogenicity [4].

Conclusions

Pregnancy in women with autoimmune inflammatory rheumatic diseases requires a structured, evidence-based approach spanning the pre-conception, pregnancy, and post-partum periods. Key principles include achieving sustained disease remission before conception, using pregnancy-compatible medications throughout gestation, engaging in shared decision-making with patients, and coordinating care through multidisciplinary teams. The 2024 EULAR update, the 2020 ACR guideline, and BSR recommendations provide a robust framework for clinical practice, though significant evidence gaps remain - particularly regarding newer biologic and targeted synthetic DMARDs. Certolizumab pegol, due to the absence of an Fc fregment (thus, having a minimal placental transfer rate), appears to be particularly safe during pregnancy

and post partum periods. With appropriate planning, monitoring, and treatment, the majority of women with AIRDs can achieve successful pregnancy outcomes.

References

[1] Queiro FDA Orange Book.FDA Orange Book.

[2] Rüegg L, Pluma A, Hamroun S, et al. EULAR Recommendations for use of antirheumatic drugs in reproduction, pregnancy and lactation: 2024 update. Ann Rheum Dis. 2025;84(6):910-926. doi:10.1016/j.ard.2025.02.023.

[3] Tarter L, Bermas BL. Expert perspectives on a clinical challenge: lupus and pregnancy. Arthritis Rheum (Hoboken, N.J.). 2024;76(3):321-331. doi:10.1002/art.42756.

[4] Sammaritano LR, Bermas BL, Chakravarty EE, et al. 2020 American College of Rheumatology guideline for the management of reproductive health in rheumatic and musculoskeletal diseases.. Arthritis Rheum (Hoboken, N.J.). 2020;72(4):529-556. doi:10.1002/art.41191.

[5] Götestam Skorpen C, Hoeltzenbein M, Tincani A, et al. The EULAR points to consider for use of antirheumatic drugs before pregnanacy and during pregnancy and lactation. Ann Rheum Dis. 2016;75(5):795-810. doi:10.1136/annrheumdis-2015-208840.

[6] Siegel CH, Sammaritano LR. Obstetrics and Gynecology 2026;:00006250-990000000-01464. doi:10.1097/AOG.0000000000006193.

[7] Silver R, Craigo S, et al. Society for maternal fetal medicine consult series no 64: systemic lupus erithematosus in pregnancy. Am J Obst Gyn. 2023;228(3):B41-B60. doi:10.1016/j.ajog.2022.09.001.

Corresponding author

Razvan Adrian Ionescu, Colentina Clinical Hospital, 3rd Internal Medicine Department, Bucharest, Romania, email: tane67@gmail.com

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