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REVIEW

Postnatal Care of Woman with Rheumatic Diseases

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ABSTRACT

Caring for women in the postnatal period can be challenging. One of the most important aspects is ensuring disease control as there is a risk of flare in the postpartum period. Other aspects of care also need to be addressed with the mother in mind such as breastfeeding or with the neonate in mind such as vaccinations or complications of the maternal condition affecting the neonate. This article highlights aspects of care that need to be addressed in the postpartum period such as flare rates, maternal wellbeing, thromboembolism, vaccinations, contraception and breast feeding.

Keywords: Breastfeeding; Contraception; Disease activity; Postnatal care; Postpartum flare; Rheumatic diseases; Rheumatology; Vaccination; Venous thromboembolism (VTE)

Key Summary Points

Postnatal care for women with rheumatic diseases requires a holistic approach.
Forty-six percent of woman with rheumatoid arthritis will flare in the postpartum period.
Live vaccinations need to be withheld if the patient is on a biologic agent throughout pregnancy.
Breastfeeding is considered safe with most biologic agents.
Venous thromboembolism (VTE) prophylaxis is essential for 10 days–6 weeks postpartum.
Contraceptive advice needs to be provided prior to discharge.

INTRODUCTION

Facing parenthood for the average human is a significant challenge full of anxiety, sleepless nights, joy and doubts. Facing parenthood with a rheumatic disease is even more challenging. Autoimmune and inflammatory rheumatic diseases affect women of child-bearing age. These

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include rheumatoid arthritis (RA), psoriatic arthritis (PSA), spondyloarthritis (SpA), systemic lupus erythematosus (SLE) and anti-phospholipid syndrome (APS).

Rheumatic diseases may increase the risk of adverse pregnancy outcomes (APO) depending on the rheumatic disease and the disease activity state. High disease activity states can result in high-risk pregnancies and complications such as fetal growth restriction, pregnancy loss, preeclampsia and preterm delivery. Therefore, a high standard of care pre-, during and post-pregnancy is needed [1–3]. By achieving good disease control throughout pregnancy, one can hopefully improve the postpartum experience.

A study exploring the information needs of women of child-bearing age with RA highlighted that women's concerns are not adequately met. Coping with rheumatic disease is superimposed on the needs of all new mothers. Concerns related to adequate information and knowledge, medication side effects and safety were raised as well as a lack of congruency between health care professionals. Many health care professionals don't feel equipped to adequately address patient concerns, and giving a consistent message to the patient is important in optimizing patient care [4].

The purpose of this article is to educate health care professionals regarding specific issues surrounding postnatal care of women with rheumatic diseases as very little information is available. In addition, there is a paucity of available specialist clinics where rheumatologists can support their obstetric colleagues. This will act as an aide memoire to remind us to address issues such as disease activity in the postnatal period, breastfeeding, vaccinations, contraception, thromboembolism and support for the mother. Important reference guides to take into account are the British Society of Rheumatology (BSR) guidelines (BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding-Part I and II); the EULAR guidelines (the EULAR points to consider for use of anti-rheumatic drugs before pregnancy and during pregnancy and lactation) and the American College of Rheumatology (ACR) guidelines on management of rheumatic and musculoskeletal diseases [16, 18, 19, 25]. This article will endeavor to address each area of concern in a practical way to empower rheumatologists looking after women with rheumatic disease in the postnatal period. This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

POSTPARTUM FLARES

One of the most common concerns for a mother with rheumatic disease is a flare at any point in pregnancy but especially in the postpartum period, as it will impact a mother's ability to look after her newborn. A flare is when there is an increase in symptoms and disease activity in the postpartum period, which is defined as from delivery up to 6 months thereafter [5]. The rate and risk factors for postpartum flares are variable depending on each condition and are summarized in Table 1 [6–8].

Disease activity in the second and third trimester is considered a risk factor for postpartum flaring. There is no association among fertility status, type of biologic used, duration of treatment and flare rates [9].

Rheumatoid arthritis has an average flare rate of 46% in the postpartum period. Risk factors include sero-positive arthritis, early discontinuation of treatment, especially anti-tumour necrosis factor-α (TNFα), and active disease at conception [7, 10]. In contrast, spondyloarthritis flare rates have been reported as high as 90%. Risk factors for flares in this group are active disease at conception and early discontinuation of anti-TNF treatment [7, 10].

The Norwegian Pregnancy Register (RevNatus) is a 17-center nationwide web based cohort study. Centers enroll patients with inflammatory rheumatic disease and followed up through pregnancy. This is the largest registry to date and provides a wealth of information [11]. In the psoriatic arthritis cohort, the postpartum flare rate is 28–55%, and in keeping with the Norwegian (Revnatus) data, this seems to be highest at 6 months postpartum. As in the spondyloarthritis group, flare rates are associated with stopping anti-TNF early [12–14].

Twenty-two percent of women with juvenile idiopathic arthritis (JIA) had a flare within 6 weeks postpartum, and 80% remained in remission or with low disease activity according to the Norwegian Register (RevNatus) [15].

SLE flares typically occur in the 6-month postpartum period. The Predictors of Pregnancy Outcome: Biomarkers in Antiphospholipid Antibody Syndrome and Systemic Lupus Erythematosus (PROMISSE) study found that in the postpartum period 27.7% of women had a mild flare and 1.7% had a severe flare. The risk of flare is dependent on disease activity in both the prepartum and antenatal period as well as stopping anti-malarial medication. Active disease 6 months prepartum is a risk factor for flare. Low C4 is a risk factor for renal flares in particular [16, 38, 39, 43]. Interestingly there is no difference in outcomes if SLE was of childhood onset [40].

The management of flares would be the same as for a non-pregnant patient provided the mother was not breastfeeding. Most postpartum flares of inflammatory arthritis and SLE can be treated with glucocorticoids. It is important to check with the mother if she is planning to breastfeed and if the medications prescribed are compatible with breastfeeding and therefore have negligible risk to the newborn.

IMMUNIZATIONS

The advent of biologic agents has changed the way we treat rheumatic conditions but these come with their own risks. Maternal IgG alone is a large protein that cannot diffuse passively across the placenta [8]. Maternal IgG is actively transferred across the placenta via the neonatal FC receptor [17]. The transfer occurs from week 20 of the second trimester. Certain biologic agents contain IgG1 proteins and therefore are also actively transported across the placenta via the neontatal FC receptor from week 20 [8, 16]. This results in the baby being exposed to the biologic agent. As per the recommended guidelines, biologic agents are stopped at the beginning of the second trimester, such as infliximab, or at the end of the second trimester, such as adalimumab and etanercept [16, 18]. This allows enough time for clearance of the biologic from the fetal circulation. If biologic agents need to be continued because of active disease, which is sometimes the case in patients with spondyloarthritis, live vaccinations need to be delayed. Clearance of biologic agents can take a minimum of 4 months from the time of the last maternal injection in the case of adalimumab and 7.3 months for infliximab. Live vaccinations should be delayed for 6 months from delivery [20].

The neonatal/infant vaccination schedule in the UK includes rotavirus and tuberculosis, which are live vaccines. These are contraindicated in infants whose mother continued anti-TNF throughout the entire pregnancy. Inactivated vaccines may be continued as per the normal vaccination schedule. Infants of mothers on non-biologic agents such as sulfasalzine and hydroxychloroquine may receive the standard vaccination schedule [8, 21].

BREASTFEEDING

A study published in 2019 found that none of the 25% of women who expressed a desire to breastfeed did so due to concerns around medication, an unwell baby and low milk supply [22]. Drug transmission in breast milk is by diffusion of the unbound drug from the mother to neonate. Drugs that are non-protein bound, non-ionized and of low molecular weight will cross into the breast milk. Considerations of breastfeeding also include the half life of the drug as the longer the half life is, the higher the concentration in the breast milk [23]. Although there is little evidence on biologic agents, they tend to have a high molecular weight therefore making transfer into the breast milk less likely. Peak levels of the drug in the breast milk will occur approximately 2 h after ingestion; however, the concentration in the infant will be less because of the function of the gastrointestinal tract. Immunoglobulin G (IgG) is broken down by the infant gastrointestinal enzymes and therefore not absorbed in significant amounts. As most biologic agents have an IgG component, the drug will be broken down in the neonatal gut and therefore not absorbed.

Table 1 A tabulated summary of post partum flares and breastfeeding in rheumatic conditions

Rheumatic condition	Risk of postpartum flare	Risk factors for flare	Drugs compatible with breast feeding	Drugs contraindicated in breastfeeding
Rheumatoid arthritis	Up to 50%	Positive anti-CCP antibody and rheumatoid factor Stopping anti-TNF therapy too early Poor disease control at conception	Conventional NSAIDs with a short half life Low-dose aspirin Prednisolone < 20 mg Sulfasalazine Hydroxychloroquine Anti-TNF agents Rituximab (c:ACR) Abatacept (c:ACR)	Methotrexate JAK inhibitors Leflunomide
Ankylosing spondylitis	Up to 90%	Stopping anti-TNF therapy too early Poor disease control at conception	Anti-TNF agents Sulfasalazine Secukinumab (c:ACR)	
Psoriatic asrthritis	28–55%	Stopping anti-TNF therapy too early Poor disease control at conception	Sulfasalazine Hydroxychloroquine Anti-TNF agents Secukinumab (c:ACR) Ustekinumab (c:ACR)	Methotrexate JAK inhibitors Leflunomide
SLE and CTD	35–70%	Active disease 6 months pre conception	NSAIDs Prednisolone Hydroxychlroquine Azathioprine Glucocorticoids IvIg Anakinra (c:ACR) Rituximab (c:ACR) Belimumab (c:ACR) Ciclosporin Tacrolimus ACE inhibitors	Mycofenelate Mofetil Cyclophosphamide
APS	Two to tenfold increase in thrombosis		Warfarin LMWH	NOACS/DOACS

Biologic agents with an IgG component are infliximab, adalimumab, etanercept and golilumab. Premature infants will have higher drug concentrations due to reduced metabolism of medication and their underdeveloped gastrointestinal tract. Janus kinase (JAK) inhibitors are oral biologic agents used to treat rheumatoid arthritis. JAK inhibitors such as tofacitinib have a lower molecular weight thus implying a risk for transfer into the breast milk [23, 24].

Prednisolone is safe during breastfeeding in doses < 20 mg. ACR advises that at higher doses mothers should delay breastfeeding for 4 h post-ingestion to allow the breast milk levels to fall. They have also highlighted certain non-anti-TNF biologic agents as "conditionally

Table 2 Risk factors for thrombosis and thromboembolism in the postpartum period

Pre-existing risk factors	Transient risk factors
Thrombophilia	Surgery in pregnancy/puerperium
Medical comorbidities such as SLE, cardiac disease, renal disease, inflammatory bowel disease, sickle cell disease, diabetes mellitus with nephrotic syndrome	Hyperemesis
	Dehydration
Age > 35 years	IVF/ART
	Ovarian hyperstimulation
BMI > 30 kg/m^2 pre- or early pregnancy	Immobility for > 3 days
Parity > 3	Systemic infection requiring admission
Smoking	Travel of > 4 h
Gross varicose veins	
Paraplegia	
Obstetric risk factors	
Multiple pregnancy	
Preeclampsia (current)	
Cesarean section	
Prolonged labor > 24 h	
Preterm birth	
Stillbirth	
Postpartum hemorrhage > 1 l	

recommended treatment." These are listed in Table 1, with a 'c' next to them [25].

Useful resources to refer to regarding medication compatibility and breastfeeding include the BSR, EULAR and ACR guidelines. Rheumatic medications that are compatible with breastfeeding are listed in Table 1. An easy access application is the lactmed application @NIH. Shared care decision-making with the mother is imperative [16, 18, 19, 25, 26, 42].

DVT PROPHYLAXIS/THROMBOSIS AND THROMBOEMBOLISM

Soon after delivery all women need to have a postpartum DVT risk assessment. Pregnant women are at a fivefold higher risk compared to non-pregnant women of developing a systemic thrombosis [27]. According to the MBRRACE study 2018, thrombosis and thromboembolism are the cause of 4% of maternal mortalities in postpartum women and the leading direct cause of maternal mortality in the UK [28, 29]. Postpartum 6-week VTE is estimated in 3–7 per 10,000 deliveries, which is a 35-fold increase compared to non-pregnant women. One study suggests that the risk levels out after 4 weeks, with another study suggesting up to 6 weeks, but in clinical practice 6 weeks is more in keeping with physiologic postpartum maternal changes [30, 31].

Part of the challenge in managing postpartum VTE is identifying and managing other contributory risk factors. Fifty percent of woman will have more than two risk factors. Common risk factors include increased maternal age, increased weight or high body mass index, smoking, preeclampsia, gestational diabetes, preterm delivery, stillbirth, multiple pregnancies, assisted reproduction techniques and cesarean sections [29, 32, 33]. See Table 2.

Treatment includes weight-based thromboprophylaxis as well as managing the other risk factors. In terms of determining treatment, the Royal College of Gynaecologist and Obstetricians (RCOG) recommend 10 days–6 weeks of treatment depending on the risk profile [34]. See Table 3.

CONTRACEPTION

This needs to be discussed soon after delivery to prevent any unplanned pregnancies. Although complete breastfeeding can cause lactational amenorrhea, it is not a reliable form of contraception, and other contraceptive options need to be explored. These options include barrier methods, progesterone-only pills and intramuscular Depo-Provera injections every 3 months as well as long-acting reversible

Table 3 Subcutaneous dosing regimen for venous thromboprophylaxis in pregnancy and the postpartum interval (This table is adapted from RCOG Green-top Guidelines No. 37a. Reducing risk of thrombosis and embolism in pregnancy and the puerperium [31])

Booking weight** (kg)	Dalteparin (first line)	Enoxaparin (second line)
< 50 kg	2500 units daily	20 mg daily
50–90	5000 units daily	40 mg daily
91–130	7500 units daily*	60 mg daily*
131–170	10,000 units daily*	80 mg daily*
> 170	75 units/kg/day*	0.6 mg/kg/day*
High prophylactic (intermediate) dose for women weighing 50–90 kg	5000 units twice daily	40 mg twice daily
Therapeutic/treatment dose	100 units/kg twice daily antenatally	1 mg/kg twice daily antenatally
	200 units/kg daily postnatally	1.5 mg/kg daily postnatally

*May be given in two divided doses

**LMWH should be given in doses titrated against the woman's booking weight. Women should be re-weighed if there appears to be a significant discrepancy between booking weight and current appearance

contraception such as progesterone implants or an intrauterine device (IUD). Combined oral contraceptive pills (COPCP) are contraindicated in anti-phospholipid syndrome because of the risk of thrombosis with estrogen. Hormonal contraception, which contains both estrogen and progesterone, can be considered safe in patients with stable SLE without any anti-phospholipid antibodies [25, 35].

Examples of intrauterine devices include the copper IUD, which can be effective for 5–-10 years, depending on the type. Mirena, the levonorgesterol-containing IUD, lasts for 5 years. Early concerns surrounding infection and immunosuppression with IUCD use are not backed by scientific evidence. Detailed contraception safety and efficacy information can be found in the recently published ACR guidelines [25].

From my clinical experience, the progesterone implant is well tolerated, lasts for 3 years and can be implanted before the mother leaves the postnatal ward. This would be in keeping with the Medicines and Healthcare products Regulatory Agency (MHRA), which advise the use of a highly effective contraception such as the implant. (https://www.gov.uk/drug-safety-update/medicines-with-teratogenic-potential-what-is-effective-contraception-and-how-often-is-pregnancy-testing-needed).

PARAMEDICAL SUPPORT

It is essential for other specialties to be involved in supporting a mother to prepare for the postnatal period. The well-being of the mother is essential in enabling her to look after a newborn baby. A women's health physiotherapist can help with pelvic floor and strengthening exercises and tips to recover sooner from the birthing process such as perineal icing and regular rest periods. This will help to reduce swelling and prevent stress incontinence as well as back pain [36, 37]. Other considerations are more practical, such as being able to change nappies with the presence of hand deformities secondary to RA. Occupational therapists may be able to help with adaptations. Resources allowing for psychologic support may also be needed because of sleep deprivation, flares and feelings of anxiety.

POSTPARTUM OBSTETRIC COMPLICATIONS

Although this article is written with the physician in mind, we must all be vigilant about possible postpartum obstetric complications that may affect the mother's clinical presentation. These include preeclampsia, eclampsia and HELLP syndrome. Active SLE is a risk factor for preeclampsia. Preeclampsia may present ante-, intra- and postpartum. In the postpartum period, women tend to be more symptomatic but early on they can be asymptomatic. Women may present with hypertension, proteinuria and edema as well as headache, epigastric pain and nausea. Hematologic abnormalities include thrombocytopenia, prolonged clotting time, raised serum creatinine levels, anemia and raised liver enzyme levels. This seems a similar presentation to women with SLE nephritis, and differentiating the two conditions can be challenging. Markers that can be used to aid diagnosis include clinical acumen, SLE serology, a drop in complement levels and red cell casts in SLE. Accurate diagnosis is important as the treatment of preeclampsia is delivery of the fetus and placenta, whereas treatment of SLE is immunosuppression. Eclampsia is a progression of preeclampsia whereby there is a seizure or coma. HELLP syndrome is a constellation of hemolysis, elevated liver enzymes and low platelet levels. In women who develop preeclampsia and eclampsia, blood pressure and renal function need to be monitored closely with avoidance of nephrotoxic drugs. Target blood pressure is $< 140/90$ mmHg [29, 40–43].

POSTPARTUM NEONATAL COMPLICATIONS

Although not within the scope of this article, neonatal complications in relation to rheumatic antibodies deserve a mention. Apart from the vaccination considerations, a small percentage (1–2%) of neonates may develop neonatal SLE. This affects neonates born to women who are Ro/SSA antibody positive and typically have SLE or Sjogren's syndrome. It can present with a skin rash, which is photosensitive, between birth and 6 weeks of age and is self-limiting. It resolves between 4 and 6 months. A more serious complication is that of congenital heart block although monitoring for this is initiated in the second trimester of pregnancy as it appears in utero between 18 and 28 weeks of gestation. Other manifestations include a transient increase in liver enzymes, hepatitis or cholestasis, anemia, neutropenia and thrombocytopenia [29, 43].

CONCLUSION

The care of women with rheumatic diseases in the postpartum period needs to include various aspects such contraception, breastfeeding, VTE and disease control. One also needs to remain vigilant regarding obstetric and neonatal complications. Access to healthcare for women in the postpartum period is essential and should form part of a standard rheumatology service. This article summarizes a practical approach to caring for women with rheumatic conditions in the postpartum period.

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