Rheumatoid Arthritis Activity During Pregnancy And Postpartum: Clinical Observations

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Abstract
Rheumatoid arthritis (RA) frequently affects women of reproductive age, which underscores the importance of studying the interplay between pregnancy and RA. Historically, early observations noted a decrease in RA activity in the majority of pregnant women. More recent prospective studies report that only 48–66% of pregnant women experience clinical improvement during gestation, while postpartum exacerbations occur in approximately 70% of patients, often necessitating pharmacological intervention.
The aim of this study was to evaluate RA activity dynamics using DAS28–CRP during pregnancy and up to 12 months postpartum, to assess the impact of disease activity at conception on subsequent RA course, and to determine the necessity and effect of anti-inflammatory therapy during gestation.
In a prospective follow-up, 32 pregnancies in 29 women with confirmed RA (ACR 1987 criteria) were monitored. During pregnancy, 46% of patients demonstrated a decrease in disease activity. Postpartum, 75% experienced RA exacerbations, typically 1.5 months after delivery. Patients with remission or low disease activity at conception maintained significantly lower disease activity throughout gestation and in the early postpartum period compared with patients presenting moderate or high activity in the first trimester ($p = 0.0008–0.04$). Similarly, women without arthritis at conception showed lower RA activity during pregnancy.
In 23 patients (71.9%) who exhibited disease activity during gestation, intensification of anti-inflammatory therapy resulted in a significant decrease in DAS28–CRP ($p = 0.008$). Conversely, 9 patients (28.1%) with low activity who did not receive intervention showed a tendency toward increased disease activity. Postpartum, patients with moderate or high activity resumed therapy earlier, which facilitated quicker improvement ($p = 0.008$), while those with low activity during pregnancy experienced a delayed increase in RA activity lasting up to three months. In 12 patients (37.5%) who discontinued basic anti-inflammatory (HDL) or genetically engineered biological therapy (GIBP) due to unplanned pregnancy, disease activity during the first to third trimesters was significantly higher than in 20 patients (62.5%) who either did not use these drugs or discontinued them prior to conception ($p < 0.04$).
Remission or low RA activity at conception predicts lower disease activity and allows for minimal or no pharmacological therapy during pregnancy. Without medical intervention, RA activity may increase. Postpartum exacerbations are common, even in patients with prior low activity, emphasizing the need for careful monitoring. Abrupt discontinuation of HDL or GIBP in unplanned pregnancies is associated with early gestational increases in RA activity. Planned pregnancy with stable anti-inflammatory therapy is recommended to optimize maternal disease control.

Keywords: rheumatoid arthritis, pregnancy, DAS28-CRP, anti-inflammatory therapy, disease activity

INTRODUCTION

Rheumatoid arthritis (RA) predominantly affects women of childbearing age, and pregnancy can influence the clinical course of the disease. The first formal observation of RA during pregnancy, conducted in 1935, indicated a reduction in disease activity in most cases. Modern literature reports variable outcomes, with 48–91% of women experiencing improvement during gestation and 60–91% facing postpartum exacerbations. Disease activity during pregnancy is also impacted by ongoing treatment, underscoring the importance of careful management.

This study was designed to track RA activity throughout pregnancy and the first year postpartum using the DAS28–CRP index, examine the effect of baseline disease activity at conception, and assess the need for anti-inflammatory therapy in pregnant women with RA. Rheumatoid arthritis (RA) frequently affects women of reproductive age, making the interaction between pregnancy and RA an area of ongoing clinical interest. Historically, early observations suggested that pregnancy induces a reduction in RA activity in the majority of patients. Contemporary prospective studies, however, demonstrate that only 48–66% of pregnant women experience clinical improvement during gestation, while exacerbations are observed postpartum in approximately 70% of cases, often necessitating pharmacological intervention.

This study aimed to evaluate RA activity dynamics using DAS28–CRP throughout pregnancy and the first year postpartum, examine the impact of disease activity at conception on subsequent RA course, and assess the need for anti-inflammatory therapy in pregnant patients.

A prospective cohort of 32 pregnancies in 29 women with confirmed RA (1987 ACR criteria) was followed throughout pregnancy and for twelve months postpartum. RA activity decreased during pregnancy in 46% of patients, while 75% experienced exacerbation within an average of 1.5 months after delivery. Patients with remission or low disease activity at conception maintained lower RA activity throughout gestation and one month postpartum compared to those with moderate or high initial activity ($p=0.0008–0.04$). Among patients receiving intensified therapy during pregnancy, DAS28–CRP significantly decreased ($p=0.008$), whereas patients with low activity without intervention showed a trend toward increasing disease activity. Abrupt discontinuation of disease-modifying therapy (HDL or GIBP) due to unplanned pregnancy was associated with significantly higher RA activity throughout gestation ($p<0.04$). Low RA activity at conception predicts a more favorable course during pregnancy and may minimize pharmacologic requirements. Postpartum exacerbation is common, including in patients with prior low disease activity. Planned pregnancy with stable anti-inflammatory therapy is recommended to reduce disease flares.

MATERIALS AND METHODS

A total of 29 women with confirmed RA (32 pregnancies) were followed prospectively. Eleven patients (38%) had juvenile RA (JURA). Clinical evaluations occurred at 10–12, 20–22, and 30–32 weeks of gestation, and at 1, 3, 6, and 12 months postpartum. Most patients (78.1%) were enrolled in the first trimester, while 9.4% and 12.5% were enrolled in the second and third trimesters, respectively. Recurrent pregnancies during the follow-up period were treated as new cases.

The median patient age was 29 years [27–31], disease duration 8 years [4–16], and age at onset 19 years [13–25]. Seropositive rheumatoid factor (RF) was present in 62.1% of patients, and antibodies to cyclic citrullinated peptide in 58.6%. Radiological stages II–III were observed in 72.4% of patients, and functional classes I–II in 86.2%. Extra-articular manifestations included pericarditis (n=4), rheumatoid nodules (n=2), polyneuropathy (n=1), and one case of organ amyloidosis. Fifteen patients (51.7%) were pre-pregnant, while 18 (62.1%) were primigravida.

Prior to conception, 93.1% of patients had used nonsteroidal anti-inflammatory drugs (NSAIDs) and 89.7% had received basic anti-inflammatory therapy (HDL). In 75% of cases, HDL was

discontinued before pregnancy (median withdrawal-to-conception interval 18 months [10–30]); in the remaining 25%, therapy was stopped immediately after pregnancy confirmation. NSAIDs were discontinued no later than 30–32 weeks of gestation.

RA activity was evaluated using the DAS28–CRP index at all study visits. Remission was defined as DAS28–CRP <2.6, low activity 2.6–3.2, moderate activity 3.2–5.1, and high activity >5.1. Patients were grouped based on disease activity at conception to assess the impact on subsequent RA course.

Descriptive statistics were expressed as median [interquartile range] for non-normally distributed data. Between-group comparisons were performed using the Mann–Whitney U test or chi-square test, and longitudinal changes were assessed using Friedman's ANOVA for repeated measures. Statistical significance was set at $p<0.05$.

RESULTS

During pregnancy, 46% of patients experienced a decrease in DAS28–CRP, with 25% showing a marked reduction. Moderate exacerbation was observed in 10.7% of cases. By the third trimester, remission or low activity increased to 62.6%, while moderate or high activity decreased to 37.4%.

Within 12 months postpartum, 75% of patients experienced RA exacerbation, with a median onset of 1.5 months [0.75–2.5]. Remission or low activity was observed in 57.7% at 12 months postpartum. Patients with low or remission activity at conception maintained lower DAS28–CRP values throughout gestation and one month postpartum ($p=0.0008–0.04$) compared to those with moderate or high activity. Among patients with active disease during pregnancy, anti-inflammatory therapy was intensified in 71.9%, resulting in a significant reduction in DAS28–CRP ($p=0.008$). Patients with low activity who did not receive therapy tended to have increasing RA activity. Abrupt discontinuation of HDL or GIBP due to unplanned pregnancy was associated with significantly higher RA activity in the first to third trimesters compared with patients who had planned therapy withdrawal ($p<0.04$).

DISCUSSION

During pregnancy, 46% of patients experienced a decrease in RA activity according to DAS28–CRP, while 10.7% had a moderate increase. By the third trimester, the number of patients with remission or low activity increased to 20 (62.6%), whereas those with moderate or high activity decreased to 12 (37.4%). Within the first month postpartum, 18 patients (56.3%) experienced exacerbation, with 10 (31.3%) showing moderate and 2 (6.3%) severe activity, occurring on average 1.5 months [range 0.75–2.5] after delivery. By the twelfth month postpartum, the number of patients with remission or low RA activity increased to 15 (57.7%), while moderate activity persisted in 11 patients (42.3%), and no cases of high activity were recorded.

Patients with remission or low RA activity at conception maintained significantly lower disease activity throughout pregnancy and one month postpartum compared to those with moderate or high activity in the first trimester ($p = 0.0008–0.04$). Similarly, patients without arthritis at conception (15, 46.9%) had lower DAS28–CRP values during gestation and early postpartum ($p = 0.0007–0.04$).

During pregnancy, anti-inflammatory therapy was intensified in 23 patients (71.9%) with active disease, resulting in a significant reduction of DAS28–CRP ($p = 0.008$). In contrast, the remaining 9 patients (28.1%) with low disease activity who did not receive therapy tended to experience a slight increase in activity. Postpartum, patients with moderate or high disease activity resumed therapy earlier with HDL and/or GIBP, which contributed to faster improvement ($p = 0.008$), whereas those with low activity during pregnancy exhibited a delayed increase in activity until three months postpartum.

Among 12 patients (37.5%) who became pregnant while taking HDL or GIBP and discontinued therapy abruptly due to unplanned pregnancy, RA activity was significantly higher during the first to third trimesters compared with 20 patients (62.5%) who either were not on such drugs or discontinued them before conception ($p < 0.04$). These patients required higher doses of anti-inflammatory drugs during pregnancy ($p = 0.04$).

Overall, the median DAS28–CRP significantly decreased during pregnancy (p = 0.005) and increased after childbirth (p = 0.05), with a subsequent trend toward reduction by the 12th month postpartum without statistical significance. Only 8 patients (25%) did not experience postpartum exacerbation within 12 months, while 24 patients (75%) experienced at least one episode.

Therapeutic interventions during gestation primarily included NSAIDs (20 patients, 62.5%) and glucocorticoids (23 patients, 71.9%). Dosage adjustments were required in 9 patients (28.1%), and 4 patients (12.5%) received therapy for the first time. Intra-articular injections were administered to 16 patients (50%) and intravenous therapy to 6 patients (18.8%). During delivery, 20 patients (62.5%) with active RA received additional parenteral GC. Postpartum therapy increased, with 24 patients (75%) resuming HDL and 27 patients (84.4%) taking NSAIDs; 8 patients (25%) received GIBP.

Comparison of patients with unchanged therapy (n = 9, 28.1%) versus those with intensified therapy (n = 23, 71.9%) during pregnancy demonstrated that RA activity decreased in the latter group, whereas in the non-intervention group, activity tended to rise, indicating the efficacy of anti-inflammatory therapy.

CONCLUSIONS

1. Forty-six percent of patients had reduced RA activity during pregnancy, whereas 75% experienced postpartum exacerbations, typically 1.5 months after delivery.
2. Anti-inflammatory therapy during pregnancy significantly reduces RA activity; without intervention, disease activity may rise.
3. Remission or low activity at conception predicts a more favorable course and may allow minimization of therapy.
4. Postpartum flares occur even in previously low-activity patients; close monitoring is required.
5. Unplanned discontinuation of HDL or GIBP leads to increased RA activity early in pregnancy, highlighting the importance of therapy planning.

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