RMD Open
Rheumatic & Musculoskeletal Diseases

SHORT REPORT

Active counselling and well-controlled disease result in a higher percentage of women with rheumatoid arthritis that breast feed: results from the PreCARA study

Erik Kemper ,[1,2] Nafise Ghalandari,[2,3] Hetty Wintjes,[3] Anneke Van Steensel-Boon,[3] Laura Kranenburg ,[3] Annemarie Mulders,[4] Hubertina Crijns,[2] Hieronymus Smeele ,[3] Radboud J EM Dolhain[3]

To cite: Kemper E, Ghalandari N, Wintjes H, *et al*. Active counselling and well-controlled disease result in a higher percentage of women with rheumatoid arthritis that breast feed: results from the PreCARA study. *RMD Open* 2022;**8**:e002194. doi:10.1136/rmdopen-2022-002194

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/rmdopen-2022-002194).

Received 3 January 2022
Accepted 5 May 2022

[1]Erasmus Medical Center, Rotterdam, The Netherlands
[2]College ter Beoordeling van Geneesmiddelen, Utrecht, The Netherlands
[3]Rheumatology, Erasmus Medical Center, Rotterdam, The Netherlands
[4]Gynaecology and Obstetrics, Erasmus Medical Center, Rotterdam, The Netherlands

Correspondence to
Nafise Ghalandari;
n.ghalandari@erasmusmc.nl

ABSTRACT

Objectives Previous research has demonstrated that patients with rheumatoid arthritis (RA) are less likely to breast feed their offspring. Treatment options for RA during lactation have expanded and the importance of counselling is recognised. The aim of the current research was to study breast feeding among women with RA who benefit from these developments.

Methods Patients were derived from the Preconceptional Counselling in Active Rheumatoid Arthritis (PreCARA) cohort. Patients were treated according to a modified treat-to-target approach aimed at remission and received pregnancy counselling, including counselling on breast feeding. Postpartum visits were scheduled at 4–6, 12 and 26 weeks post partum. Prevalence of breast feeding at each postpartum visit was compared with a historical reference cohort (Pregnancy-induced Amelioration of Rheumatoid Arthritis cohort) and the general population.

Results Data on 171 pregnancies were available for the current analysis. 120 (70.2%) patients with RA initiated breast feeding. 103/171 (60.2%), 68/171 (39.8%) and 45/171 (26.3%) patients with RA breast fed their offspring at 4–6, 12 and 26 weeks post partum, respectively. These percentages were higher at all postpartum visits compared with the historical reference cohort ($p<0.001$). In comparison with the general population, the rates were similar at each time point.

Conclusion Patients with RA in the PreCARA cohort were more likely to breast feed their offspring compared with patients with RA in the historical reference cohort. The breastfeeding rates observed were similar to breastfeeding rates among women in the general population. The increase in breast feeding among patients with RA may be due to the extension of lactation-compatible medication and pregnancy counselling.

KEY MESSAGES

⇒ The advantages of breast feeding have been demonstrated in many studies.
⇒ Previously, women with RA were less likely to breast feed their offspring compared with women in the general population.
⇒ Women with RA who receive counselling and are treated according to a modern treatment approach are as likely as women in the general population to breast feed their offspring.
⇒ This study suggests the importance of a combination of counselling and a modern treatment approach for women with RA.

INTRODUCTION

The advantages of breast feeding over formula feeding have been demonstrated in many studies.[1] These benefits of breast feeding are even more pronounced in children with low birth weight.[2]

Previous research has demonstrated that women with rheumatoid arthritis (RA) are less likely to breast feed. The main reason for discontinuing breast feeding was the restart of disease-modifying antirheumatic drugs (DMARDs). Importantly, in women with RA, high disease activity during pregnancy is associated with low birth weight.[3] Additionally, such women are less likely to breast feed.[1]

The treatment options for RA that are compatible with breast feeding have increased and now include tumour necrosis factor (TNF) inhibitors.[4] Additionally, the importance of counselling on pregnancy and lactation is recognised.[5]

It is currently unknown if patients with RA who underwent pregnancy counselling and were treated according to a modern treatment approach, with the use of TNF inhibitors, are more likely to breast feed. The primary aim of this study was to investigate

breast feeding among women with RA who benefit from these developments.

METHODS

Study population

The study population consisted of patients with RA derived from the Preconceptional Counselling in Active Rheumatoid Arthritis (PreCARA) study (clinicaltrials.gov registration: NCT01345071) (first inclusion in 2011).[5] For the current analysis, patients who had at least one postpartum visit were included (last visit: 11 September 2020).

Treatment and pregnancy counselling

Patients included in the PreCARA study were treated according to a modified treat-to-target approach aimed at remission or low disease activity.[5] Patients in the PreCARA cohort are enrolled in a specialised multidisciplinary clinical path for pregnancy among women with rheumatic diseases and undergo intensive counselling on pregnancy and breast feeding from specialised rheumatology nurses. This counselling included practical advice on positioning during breast feeding and use of appliances such as a nursing pillow and a breast pump.

Data collection

Visits were scheduled during each trimester and post partum at 4–6, 12 and 26 weeks. During all visits, data on medication use, disease activity (28-joint count Disease Activity Score using C reactive protein levels)[6 7] and functionality (Stanford Health Assessment Questionnaire[8]) were collected. During the postpartum visits, also data on breast feeding were collected, including the duration and reasons for discontinuation.

Data analysis

Rates of women who breast fed their offspring at the three postpartum visits were calculated. The study population was compared with two reference groups. The first reference group consisted of 249 patients with RA who were included in the Pregnancy-induced Amelioration of Rheumatoid Arthritis (PARA) study between 2002 and 2010.[1 9] The second reference group consisted of 32.532 women who participated in a population-based study on breast feeding in the Netherlands conducted in 2018.[10]

Due to the difference in the percentage of women who were lost to follow-up between the PARA and PreCARA cohort and since one could not exclude that women who were lost to follow-up were less likely to breast feed, all women who were lost to follow-up were included in the analyses and considered not to breast feed. It was chosen to analyse the data according to a so called 'worst case' scenario in order to reduce the impact of attrition bias.[11]

Statistical analysis

Descriptive statistics were presented as number (%), mean (SD) or median (IQR). Low birth weight was defined as a birth weight of <2500 g.[12] Early discontinuation of breast feeding was defined as stopping before 12 weeks post partum. Breastfeeding percentages were compared between the study population and the reference groups and between subgroups. t-Tests, two proportion tests and χ^2 tests were used if appropriate.

Stata software V.16.0 was used for all statistical analyses. P values of <0.05 were considered statistically significant.

RESULTS

Baseline characteristics

Data from 171 pregnancies from the PreCARA study were available for the current analysis. The historical reference cohort consisted of 249 patients derived from the PARA study. Baseline characteristics of both cohorts are shown in table 1.

Loss to follow-up

In the PARA cohort, 2%, 2% and 9% of patients were lost to follow-up at weeks 4–6, 12 and 26, vs 5%, 16% and 27% in the PreCARA cohort, respectively.

Breast feeding

Numbers and rates of breastfeeding women in the PreCARA cohort and the two reference cohorts are depicted in table 2 and supplemental figure 1. Of the women who breast fed at 4–6 weeks post partum in the PreCARA cohort, 53/103 (51.5%) did so exclusively; 20/103 (19.4%) did so partially; and for 30/103 (29.1%) women, these data were missing. These numbers were 30/68 (44.1%), 11/68 (16.2%) and 27/68 (39.7%), respectively, at 12 weeks post partum, and 15/45 (33.3%), 10/45 (22.2%) and 20/45 (44.4%), respectively, at 26 weeks post partum.

In the PreCARA cohort, 15 (8.8%) women delivered an infant with a birth weight lower than 2500 g. Of these 15 women, 12 (80%) breast fed at 4–6 weeks post partum (p=0.051 vs birth weight ≥2500 g), 8 (53.3%) breast fed at 12 weeks post partum (p=0.132 vs birth weight ≥2500 g); and 4 (26.6%) breast fed at 26 weeks post partum (p=0.980 vs birth weight ≥2500 g). In the historical reference cohort, 23 (9.2%) women delivered an infant with a birth weight lower than 2500 g. Breastfeeding percentages in this group were 26.1% (6/23) at 4–6 weeks, 17.4% (4/23) at 12 weeks and 4.4% (1/23) at 26 weeks post partum (p<0.001 vs PreCARA cohort at each time point). In the general population, 52% of women with low-birth-weight infants initiated breast feeding; data on breast feeding at later time points were unavailable.

Reasons for discontinuation

Reasons for discontinuation of breast feeding are summarised in table 3. One out of 14 (7%) stopped breast feeding before week 26 post partum because of medication, while the prescribed medication (prednisone) was compatible with breast feeding.

Table 1 Descriptive statistics of women with RA included in the PreCARA cohort (N=171), PARA cohort (N=249) and the general population cohort (N=32 532*)

Variable	PreCARA cohort	PARA cohort	General population	P value
Maternal age at delivery (years), mean (SD)	31.7±3.9	32.8±3.8	Unavailable	0.050
Disease duration at inclusion (years), median (IQR)	6.5 (3.2–10.7)	4.9 (2.2–9.8)	n/a	0.032
DAS28-CRP, third trimester, mean (SD)	2.2±0.7	3.4±1.1	n/a	<0.001
DAS28-CRP, 12 weeks post partum, mean (SD)	2.2+0.8	3.6±1.2	n/a	<0.001
HAQ, third trimester, median (IQR)	0.50 (0.13–0.88)	0.75 (0.25–1.25)	n/a	<0.001
Nulliparity	76 (44.4)	124 (51.5)	5412 (48)	0.153
RF and/or ACPA positive	151 (88.3)	186 (74.7)	n/a	<0.001
Presence of erosions	54 (31.6)	150 (60.2)	n/a	<0.001
Birth weight (g), mean (SD)	3217±550	3324±594	Unavailable	0.063
Birth weight <2500 g	15 (8.8)	23 (9.2)	602 (5)	0.888
Preterm delivery (gestational age <37 weeks)	19 (11.1)	28 (11.2)	692 (6)	0.975
Education level (years), median (IQR)	16 (14–18)	15 (13–17)	Unavailable	0.001
Smoking	6 (3.5)	22 (8.8)	Unavailable	0.032
Medication post partum††				
Methotrexate	44 (25.7)	104 (41.8)	n/a	<0.001
Prednisone	69 (40.4)	107 (43.0)	n/a	0.596
Hydroxychloroquine	93 (54.5)	24 (9.6)	n/a	<0.001
Sulfasalazine	101 (59.1)	87 (34.9)	n/a	<0.001
TNF inhibitors‡‡	80 (46.8)	33 (13.3)	n/a	<0.001
Tocilizumab	9 (5.3)	0 (0.0)	n/a	<0.001
Golimumab	1 (0.6)	0 (0.0)	n/a	<0.001
Abatacept	2 (1.2)	0 (0.0)	n/a	<0.001
Azathioprine	3 (1.8)	4 (1.6%)	n/a	0.876
Leflunomide	3 (1.8)	3 (1.2)	n/a	0.613

Values are numbers (%) unless indicated otherwise.
*Not all 32 532 participants were available at each time point.
†Any use during 6 months after delivery, either alone or in combination.
‡Certolizumab pegol, etanercept, adalimumab or infliximab.
ACPA, anticitrullinated protein antibody; DAS28-CRP, 28-joint count Disease Activity Score using C reactive protein levels; HAQ, Health Assessment Questionnaire; PARA, Pregnancy-iinduced Amelioration of Rheumatoid Arthritis; PreCARA, Preconceptional Counselling in Active Rheumatoid Arthritis; RA, rheumatoid arthritis; RF, rheumatoid factor; TNF, tumour necrosis factor.

DISCUSSION

In this study, we show that women with RA in the PreCARA cohort are more likely to breast feed compared with a historical reference cohort and that breastfeeding rates are comparable with the general population.

Over the past decade, several aspects of the treatment of RA before, during pregnancy and post partum have changed. Before pregnancy, women may have received more intensive treatment, resulting in less physical disability when entering pregnancy, as can be learnt from

Table 2 Numbers and rates of breastfeeding women (either partial or exclusive) at 4–6 weeks, 12 weeks and 26 post partum for the study population, the historical reference cohort and the general population

	PreCARA cohort n=171	Historical reference cohort (PARA) n=249	General population n=32 532*
Weeks 4–6, n (%)	103 (60.2)	108 (43.4)†	11 152 (59)
Week 12, n (%)	68 (39.8)	65 (26.1)†	7 731 (41)
Week 26, n (%)	45 (26.3)	23 (9.2)†	4 205 (28)

*Not all 32 532 participants were available at each time point: 18 928 participants were available at weeks 4–6, 18 620 at week 12 and 15 281 at week 26.
†P value <0.001 compared with the PreCARA cohort.
PARA, Pregnancy-iinduced Amelioration of Rheumatoid Arthritis; PreCARA, Preconceptional Counselling in Active Rheumatoid Arthritis.

Table 3 Reasons for discontinuation of breast feeding in patients who initiated breast feeding but stopped before week 26 post partum (n=74)

Reason for discontinuation	<6 weeks (n=32)	6–12 weeks (n=19)	12–26 weeks (n=23)	Total (n=74)
Medication	3 (9%)	6 (32%)	5 (22%)	14 (19%)
Maternal reasons				
Not enough milk	13 (41%)	7 (32%)	9 (39%)	29 (39%)
Too painful/active disease	5 (16%)	8 (42%)	0 (0%)	13 (18%)
Too much effort	3 (9%)	4 (21%)	1 (4%)	8 (11%)
Work-related	0 (0%)	1 (5%)	3 (13%)	4 (5%)
Mastitis	3 (9%)	0 0(%)	0 (0%)	3 (4%)
Breast cancer screening	0 (0%)	0 (0%)	2 (9%)	2 (3%)
No desire to breast feed	1 (3%)	1 (5%)	0 (0%)	2 (3%)
Shingles	0 (%)	0 (%)	1 (4%)	1 (1%)
Thyroid-related medication	1 (3%)	0 (%)	0 (0%)	1 (1%)
Child-related reasons				
Struggle to latch	4 (13%)	0 (0%)	0 (0%)	4 (5%)
Failure to thrive	1 (3%)	2 (11%)	0 (0%)	3 (4%)
Child refused to drink	0 (0%)	0 (0%)	2 (9%)	2 (3%)
Unknown reasons	5 (16%)	1 (5%)	3 (13%)	9 (12%)

Some patients discontinued breast feeding for more than one reason.

the lower percentage of women with erosive disease in the PreCARA cohort compared with the PARA cohort. Regarding pregnancy and the postpartum period, knowledge on the safety of DMARDs, including TNF inhibitors, during pregnancy and lactation has increased.[1 4] Consequentially, disease activity is better manageable after delivery, and less patients require the use of medication that is currently considered lactation-incompatible, such as methotrexate or biologicals other than TNF inhibitors(TNFi). All these factors might have contributed to a higher percentage of women that breast feed in the PreCARA cohort.

Furthermore, the importance of counselling in the management of rheumatic diseases in patients before, during and after pregnancy is widely recognised nowadays.[13 14] The combination of expanded treatment options, lower disease activity and counselling could be responsible for the observed increase in breastfeeding rates. However, due to the design of the study, it was not possible to investigate the effects of these components individually.

Breast feeding is especially beneficial in low-birth-weight infants.[2] In addition to regular benefits, breast feeding in low-birth-weight infants is associated with a decreased incidence of illnesses such as sepsis, with improved neurodevelopmental outcomes.[2] In our study, women who gave birth to a low-birth-weight child were more likely to breast feed than women who gave birth to a child with normal birth weights. In contrast, women in the historical reference cohort who gave birth to a low-birth-weight child were less likely to breast feed their offspring.[1] Possible explanations for the higher breastfeeding rates in our study are better treatment options and the fact that women in the PreCARA cohort were made aware of the increased benefits of breast feeding low-birth-weight infants.

Literature on breast feeding among patients with rheumatic diseases is scarce. Recently, Ikram *et al* published a paper on breast feeding among women with rheumatic diseases.[15] In their study, 222 out of 264 (85%) women initiated breast feeding. Of these women, 172 (65%) still breast fed at the postpartum visit, which was scheduled at an average of 7.6 (SD 4.6) weeks post partum.[15] The latter percentage is somewhat difficult to compare to our results due to the large variation in the number of weeks after birth but appears slightly higher. Our observations are in line with literature on other chronic diseases, such as Crohn's disease. In Crohn's disease, women are as likely as the general population to initiate breast feeding.[16]

Medication use as a reason for discontinuation was reported less often in the current study compared with the historical reference cohort (19% vs 58%). Furthermore, only one patient stopped breast feeding because of medication, although it was compatible with lactation. In the historical reference cohort, this percentage was 42%. This difference highlights the importance of counselling on the use of DMARDs post partum.

We used an updated general population reference group compared with the original publication of our historical reference cohort.[1] The number of women in the general population that breast fed their offspring at 4–6 weeks and 12 weeks post partum was comparable in both surveys.[10 17] However, at 26 weeks post partum, the breastfeeding rates were 41% in the 2005 survey and 28%

in the 2018 survey. This difference is explained by a more representative sample of the general population in the 2018 survey with regard to ethnic diversity and educational level.[10]

Some limitations of our study must be considered. Most importantly, an observed association does not necessarily mean that there is a causation, especially in observational studies. It therefore cannot be ruled out that the observed difference between the cohorts is due to unadjusted confounding. The current study population was treated in a tertiary hospital specialising in the treatment of RA during pregnancy. Another limitation of our study is the missing data in particular on partial or exclusive breast feeding and patients who did not complete all three postpartum visits. However, a subgroup analysis with patients who completed all postpartum visits showed similar breastfeeding rates at all postpartum visits compared with patients who did not complete all three postpartum visits.

In conclusion, women with RA in the PreCARA cohort are more likely to breast feed their offspring compared with patients with RA in a historical reference cohort. The breastfeeding rates we observed are comparable to breastfeeding rates among women in the general population. Our study highlights the importance of counselling before, during and after pregnancy. This, in combination with the increased availability of lactation-compatible DMARDs and better controlled disease in the postpartum period, may have contributed to the increase in breast feeding among patients with RA.

Contributors All authors met the authorship criteria. They had a substantial contribution to the conception or design of the work (HS and RJED) or the acquisition (RJED, HW and AVS-B), analysis (NG, EK, HS and RJED) or interpretation of data for the work (all authors); were involved in revising a draft of this work; gave the final approval of this version to be published; and were accountable for all aspects of the work in ensuring accuracy and integrity.

Funding UCB provided financial support to this investigator-initiated study. This work was also supported by the Dutch Arthritis Foundation (ReumaNederland) (project number: LLP-26), a non-profit organisation.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval The Preconceptional Counselling in Active Rheumatoid Arthritis study (MEC-2011–032) and the Pregnancy-iinduced Amelioration of Rheumatoid Arthritis study (MEC-214.320/2002/117) were approved by the medical ethics committee of the Erasmus Medical Center. The participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iDs
Erik Kemper http://orcid.org/0000-0003-3540-9896
Laura Kranenburg http://orcid.org/0000-0001-5201-0938
Hieronymus Smeele http://orcid.org/0000-0001-7724-7712

REFERENCES

1 Ince-Askan H, Hazes JMW, Dolhain RJEM. Breastfeeding among women with rheumatoid arthritis compared with the general population: results from a nationwide prospective cohort study. *J Rheumatol* 2019;46:1067–74.
2 Gharib S, Fletcher M, Tucker R, *et al*. Effect of dedicated lactation support services on breastfeeding outcomes in extremely-low-birth-weight neonates. *J Hum Lact* 2018;34:728–36.
3 de Man YA, Hazes JMW, van der Heide H, *et al*. Association of higher rheumatoid arthritis disease activity during pregnancy with lower birth weight: results of a national prospective study. *Arthritis Rheum* 2009;60:3196–206.
4 Götestam Skorpen C, Hoeltzenbein M, Tincani A, *et al*. The EULAR points to consider for use of antirheumatic drugs before pregnancy, and during pregnancy and lactation. *Ann Rheum Dis* 2016;75:795–810.
5 Smeele HT, Röder E, Wintjes HM, *et al*. Modern treatment approach results in low disease activity in 90% of pregnant rheumatoid arthritis patients: the PreCARA study. *Ann Rheum Dis* 2021;80:859–64.
6 Prevoo ML, van 't Hof MA, Kuper HH, *et al*. Modified disease activity scores that include twenty-eight-joint counts. development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. *Arthritis Rheum* 1995;38:44–8.
7 Andreoli L, Gerardi MC, Fernandes M, *et al*. Disease activity assessment of rheumatic diseases during pregnancy: a comprehensive review of indices used in clinical studies. *Autoimmun Rev* 2019;18:164–76.
8 Bruce B, Fries JF. The Stanford health assessment questionnaire: a review of its history, issues, progress, and documentation. *J Rheumatol* 2003;30:167–78.
9 de Man YA, Dolhain RJEM, van de Geijn FE, *et al*. Disease activity of rheumatoid arthritis during pregnancy: results from a nationwide prospective study. *Arthritis Rheum* 2008;59:1241–8.
10 Engelse O, Van Dommelen P. *Rapport Peiling Melkvoeding: Nederlands Centrum Jeugdgezondheid*, 2018.
11 Bankhead C, Aronson JK, Nunan D. *Catalogue of bias*, 2017.
12 World Health Organization. *International statistical classification of diseases and related health problems. 10th revision*. 2016. Fifth edition. Geneva: World Health Organization, 2015.
13 Østensen M. Preconception counseling. *Rheum Dis Clin North Am* 2017;43:189–99.
14 Nalli C, Galli J, Lini D, *et al*. The influence of treatment of inflammatory arthritis during pregnancy on the long-term children's outcome. *Front Pharmacol* 2021;12:626258.
15 Ikram N, Eudy A, Clowse MEB. Breastfeeding in women with rheumatic diseases. *Lupus Sci Med* 2021;8:e000491.
16 van der Woude CJ, Ardizzone S, Bengtson MB, *et al*. The second European evidenced-based consensus on reproduction and pregnancy in inflammatory bowel disease. *J Crohns Colitis* 2015;9:107–24.
17 L C, JV W. *Peiling melkvoeding van zuigelingen 2005: Borstvoeding in Nederland en relatie Met certificering door stichting Zorg voor Borstvoeding: TNO Kwaliteit van level*, 2006.