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In rheumatoid arthritis fewer women breastfeed their offspring compared with women from the general population; results from a nationwide prospective cohort study

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ABSTRACT

Objectives. The World Health Organization recommends to exclusively breastfeed infants until the age of six months. The first objective was to compare breastfeeding frequencies and time of cessation between women with rheumatoid arthritis(RA) and the general population. Second, to identify why patients with RA discontinue breastfeeding.

Methods. This study was embedded in the Pregnancy induced Amelioration of Rheumatoid Arthritis study, a nationwide prospective cohort study. From 2002–2008 in total 249 pregnancies were followed from pregnancy until 6 months postpartum. Data on lactation and medication use were collected. Proportion tests were used to compare percentages of breastfeeding between the study population and the general/reference population.

Results. At 4-6, 12 and 26 weeks postpartum 43%, 26% and 9% of the RA patients breastfed their offsprings respectively, compared with 63%, 46% and 41% in the general population(p-values<0.001). The main reason for women to discontinue breastfeeding was the restart of medication(n=129, 58.6%). Nevertheless, more than 40% of these patients restarted medication that was considered compatible with breastfeeding.

Conclusions. This large prospective study demonstrates that RA is associated with lower proportions of women breastfeeding their offspring and earlier cessation compared with the general population. A considerable amount of patients discontinue breastfeeding so that they could start medication, despite the fact that many of the medications are considered safe to use during lactation. Using the results of this study, intervention strategies supporting RA patients who wish to breastfeed may be developed.

Keywords: Breastfeeding, rheumatoid arthritis, pregnancy, medication.

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Research on the impact of pregnancy on rheumatoid arthritis(RA) and the consequences of RA on pregnancy has gained interest in the last years. However, breastfeeding in RA patients is a neglected area, since there are limited numbers of studies on this subject. There are no studies available that compare breastfeeding frequency and duration in RA with the general population Considering lactation in RA patients, one prospective study, that focused on disease activity in relation with breastfeeding, showed worse disease activity 6 months postpartum in first-time breastfeeding women compared with non-breastfeeding women[1].

The World Health Organization(WHO) recommends to exclusively breastfeed infants until the age of six months, and to continue breastfeeding until two years(or beyond) alongside complementary foods[2]. Besides being the most optimal infant nutrition and improving the bond between mother and child[3, 4], breastmilk also benefits for long-term health[2][5], [6][7, 8][9, 10]. Breastfeeding especially has major benefits for high-risk infants born prematurely[5]. Since RA may have a negative impact on pregnancy outcome[11], breastfeeding might be utmost important for their offsprings.

In view of the increased risk of a flare of RA within 3 months postpartum, medication is often restarted after delivery[12]. Safety data on the use of most antirheumatic drugs during lactation are absent or limited[13]. At the time this study was conducted, medication that was considered safe during lactation were conventional Disease Modifying AntiRheumatic Drugs(DMARDs) like hydroxychloroquine, sulfasalazine, and anti-inflammatory drugs like prednisone and non-selective NSAIDs[14]. Drugs that were advised to be avoided during

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lactation included methotrexate(MTX) and leflunomide. Biologicals, all selective COX II inhibitors and azathioprine were also not recommended to be prescribed during lactation(at the time this study was conducted)[14].

The aims of the current prospective study were first to compare frequency and duration of breastfeeding in women with RA with the general population. Second, to identify reasons why RA patients discontinue breastfeeding. Finally, to identify clinical factors in 3rd trimester during pregnancy associated with discontinuation of breastfeeding within three months postpartum. This study will help to understand the impact of RA on lactation, and to develop intervention strategies to support RA patients who wish to breastfeed.

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PATIENTS AND METHODS

Study Population

The study cohort consisted of women who participated in the Pregnancy induced Amelioration of Rheumatoid Arthritis(PARA) study, a nationwide prospective cohort study from the Netherlands with an inclusion period from 2002 to 2008(last visit in 2010), described in detail previously[15]. Patients were recruited by their rheumatologist if they met the American College of Rheumatology 1987 revised criteria for RA[16]. Inclusion was possible if patients had a wish to conceive, or when they were already pregnant(preferably in first trimester). In total, 249 pregnancies were available for the current analysis[17].

The reference group consists of 3009 women recruited throughout the Netherlands in 2005 for a population-based study on breastfeeding, representative of the general population at that time[18]. Women were eligible for inclusion if their infant was aged 6 months or younger.

Data collection

In the PARA-study, patients were visited by a research nurse at home before pregnancy, three times during pregnancy and three times postpartum(6, 12 and 26 weeks). At all time-points a physical examination was performed and information on mother(e.g. disease activity, functionality, medication) and child was collected. Postpartum, data on child feeding was collected using questionnaires. These included questions on the start and duration of breastfeeding, on exclusive breastfeeding or combined with infant formula, or exclusively formula, and on the reason for discontinuing breastfeeding(restart of medication, maternal/child related reasons, or a combination). Maternal reason were: no desire to,

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mastitis, work, too much effort, not enough milk, breast surgery. Child related reasons were: struggle to latch, failure to thrive, illness.

The Disease Activity Score based upon 3 variables; swelling and tenderness in 28 joints and a C-Reactive Protein(DAS28-CRP(3)) was used to measure disease activity[19, 20]. Remission was defined as a DAS28-CRP(3)<2.6, low disease activity as ≥2.6 to <3.2[15]. In 10 patients, the DAS28-CRP(3) in third trimester was missing. Since the correlation between DAS28-CRP(3) in second and third trimester was high(0.7), it was substituted with the DAS28-CRP(3) from second trimester in these patients.

As a measure for functionality, the conventional health assessment questionnaire(HAQ) score was determined using the validated Dutch translation of the Stanford HAQ, which considers the use of devices and aids[20-22]. Rheumatoid Factor(RF) and anti-citrullinated protein antibody(ACPA) were measured in the 3rd trimester.

In the reference group questionnaires were used to determine among others frequency and duration of breastfeeding, exclusive breastfeeding or combined with infant formula, or exclusively infant formula.

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Statistical Analysis

Descriptive statistics were calculated as numbers, percentages, means, medians, standard deviation scores(SDSs) and interquartile ranges(IQRs). Proportion tests were used to compare percentages of breastfeeding between the study population and general/reference population. Chi squared tests were used to compare frequencies between groups. Student's *t*-tests were used to compare DAS28-CRP(3) between breastfeeding and non-breastfeeding patients. Subgroups based on birthweight were created(birthweight<2500g and ≥2500g) . Chi squared tests were used to compare breastfeeding frequencies between low and normal birthweight infants.

For the analysis of early cessation of breastfeeding a multivariable logistic regression model was built. Covariables with a p-value<0.2 in univariable analysis were used in the multivariable model. After that, the model was fitted step-by-step using backwards selection of variables with p-values>0.2. The dependent variable was discontinuation of breastfeeding before 12 weeks postpartum. Independent variables were the HAQ in the 3rd trimester, the autoantibody status, use of MTX in the past, the socioeconomic status(SES) based on educational level, prednisone use in the 3rd trimester, sulfasalazine use in the 3rd trimester, the presence of erosions, DAS28-CRP(3) in 3rd trimester, maternal smoking periconceptional and/or during pregnancy, the visual analogue scale for global health(VAS GH) in 3rd trimester, maternal age and parity.

A subgroup analysis was performed including only the first participation of the patients in the PARA-study. Breastfeeding frequencies were once again analyzed using Chi squares tests, and the regression model was repeated in this group.

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Statistical significance was defined as p ≤0.05. All statistics were performed using STATA software version 15.1 for Windows.

Ethics

This study is in compliance with the Helsinki Declaration. The Medical Ethics Committee at the Erasmus Medical Center Rotterdam, the Netherlands, approved the PARA study(MEC-214.320/2002/117). All participants provided written informed consent.

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RESULTS

Participants

In the PARA-study, in total 369 patients were included, which resulted in 256 successful pregnancies. The DAS28-CRP(3) in the second and third trimester was missing in 7 pregnancies. After exclusion of these, in total data on 249 pregnancies from 216 women were available for the current analysis. Descriptive statistics of the study population are shown in table 1. The mean maternal age at delivery was 32.8 years and the median duration of RA was 4.9 years. The mean DAS28-CRP(3) was 3.4 in the third trimester.

Since the median HAQ in the third trimester was 0.75(IQR= 0.25 – 1.25), the HAQ was dichotomized to lower(<0.75) and higher(≥0.75) HAQ. This resulted in 114 patients(45.8%) with lower, and 135 patients(54.2%) with higher HAQ.

In total, 186(74.7%) were classified as RF and/or ACPA positive. Approximately half of the patients had high SES based on educational level(university of applied sciences and academic university education). In total 22 patients(8.8%) smoked periconceptional or during pregnancy.

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Breastfeeding

In total(exclusive and partial breastfeeding combined), 108 patients(43%) breastfed their offspring until at least 4-6 weeks, 65(26%) until at least 12 weeks and 23(9%) until at least 26 weeks postpartum compared with 63%, 46%, and 41% respectively in the reference population(all p-values<0.001)(table 2). In the PARA study, breastfeeding frequency and duration was not different between nulliparous and multiparous RA patients.

Since breastmilk especially has benefits for infants with low birth weight[5], subgroups based on birthweight were created in the offsprings born to women with RA from the PARA-study, resulting in 23 infants with a birthweight <2500g and 226 ≥2500g. Only 26.1%, 17.4% and 4.4% of the offsprings <2500g were breastfed at 4-6 weeks, 12 weeks and 26 weeks respectively compared with 45.1%, 27.0% and 9.7% respectively in the offsprings with a birthweight ≥2500g(not significant).

In total, 33 women participated more than once in this study. To exclude possible selection bias in the obtained results, a subgroup analysis, including only the first participation of the patients(n=216) was performed. Similar results in breastfeeding frequency and duration were obtained(data not shown).

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Reasons for discontinuation

In total, 223 patients discontinued breastfeeding over the course of 26 weeks. In 129 patients(58.6%), the reason for discontinuation of breastfeeding was restart of medication(table 3). From these 129 patients, in total 86 (61.0%) reported that the reason for cessation was restart of medication before 6 weeks, 28 patients(65.1%) between 6-12 weeks and 15 patients(41.7%) between 12-26 weeks postpartum. In 76/129 patients(58.9%) medication that was considered not compatible with lactation(at that time this study was conducted) was initiated. The other 53 patients(41.1%) received(a combination of) prednisone(49.1%), sulfasalazine(39.6%), hydroxychloroquine(18.9%), and/or non-selective NSAIDs(37.7%), all considered safe to use during lactation.

In total, 94 patients(42.2%) reported reasons for cessation, other than restart of medication. From these, the majority(n=77, 81.9%) included maternal reasons, e.g. “not enough milk”(35.1%) and “no desire to”(17.0%). As for child related reasons(n=15, 16.0%), the majority included “struggle to latch”(7.4%) and “failure to thrive”(6.4%),(see table 3). In the general population(Netherlands 2000-2003[23]), cessation due to “not enough milk”(including concern about the amount of milk), “problems relating to breasts and/or nipples”, and “health problems in the infant” were comparable with the results from this study. Work related cessation was reported in 7.4% of the patients in this study(in patients with reasons other than restart of medication) compared with 13.9% in the general population(p-value<0.05)[23].

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As for the subgroups based on birth weight, approximately half of the patients with an offspring <2500g reported discontinuation due to maternal reasons and the other half due to restart of medication. These patients received MTX or a combination(54.5%), sulfasalazine or a combination(27.3%), prednisone or a combination(63.6%), hydroxychloroquine or a combination(18.2%), and non-selective NSAIDs or a combination(27.3%).

Disease activity and medication use

The DAS28-CRP(3) changed from 3.1 to 3.4 to 3.0 at 6, 12, and 26 weeks after delivery in breastfeeding and from 3.5 to 3.7 to 3.5 in non-breastfeeding patients(p value at all time points between the two groups < 0.05).

Medication use postpartum is shown in table 4. Overall, patients who were not breastfeeding received more medication compared with patients who were breastfeeding. MTX and leflunomide were exclusively prescribed to non-breastfeeding patients.

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Early discontinuation

For clinical purposes the HAQ in third trimester was dichotomized at the median for easier interpretation(<0.75 and ≥0.75). In univariable analyses, the HAQ, presence of autoantibodies, smoking periconceptional or during pregnancy, MTX use in the past, SES , prednisone use in third trimester, the presence of erosions and the DAS28-CRP(3) in third trimester were associated with discontinuation <12 weeks(p-values<0.20)(table 5).

In the multivariable model, only the HAQ in the 3rd trimester, presence of autoantibodies and smoking were statistically significant(OR 3.7, 3.2, and 5.9 respectively, and p-values<0.001, 0.003, and 0.032 respectively), see table 5. Patients with higher HAQ, patients who were autoantibody positive and patients who smoked periconceptional or during pregnancy were more likely to discontinue breastfeeding within 12 weeks postpartum.

Patients with a HAQ ≥0.75 were more likely to restart MTX, leflunomide and biologicals at 6 or 12 weeks postpartum compared with patients with a HAQ <0.75(p=0.001). In addition, in patients with a HAQ ≥0.75 the disease activity postpartum was higher compared with patients with a HAQ<0.75(DAS28-CRP(3) 3.8 vs 3.3, p-value=0.001).

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Also, patients who were autoantibody positive were more likely to restart MTX, leflunomide and biologicals at 6 or 12 weeks postpartum compared with patients who were autoantibody negative(p= 0.019). The autoantibody positive patients had higher disease activity postpartum compared with autoantibody negative patients(DAS28-CRP(3) 3.7 vs 3.2, p-value<0.001).

In the subgroup including only the first participation of the patients(n=216), similar results for the regression models were obtained(data not shown).

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DISCUSSION

In this large nationwide prospective study, we have shown that women with RA are less likely to breastfeed their offsprings compared with women from the general(reference) population. More than half(57%) of the patients discontinue breastfeeding before 6 weeks. At 12 weeks only 26% of the patients were still breastfeeding(exclusively and partially combined) compared with 46% in the reference population. At 6 months postpartum the difference was extremely large(9% vs 41% respectively).

The majority of the patients reported that they discontinued breastfeeding due to restart of medication. However, more than 40% of the patients ceased breastfeeding due to start of medication that was considered compatible with lactation, according to guidelines at the time this study was conducted(prednisone, sulfasalazine, hydroxychloroquine, and/or non-selective NSAIDs). Cessation while using compatible medication was therefore not related to one specific antirheumatic drug. The only exception was hydroxychloroquine, which was prescribed to 4 women during pregnancy, and none during breastfeeding. However, due to the small numbers, a coincidence cannot be ruled out. This cessation of breastfeeding while using compatible medication could therefore perhaps be due to a general fear for taking medication when breastfeeding, a lack of knowledge, or generic preferences of women to not take any medication whilst breastfeeding. Unfortunately, in this study it was not assessed whether patients themselves did not feel comfortable to breastfeed when taking medication or whether this was discouraged by their physician. Retrospectively collecting data on this subject was not possible, since our study was a nationwide prospective study, and patients were recruited by rheumatologists from different hospitals, all over the country. In addition, we did not have

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informed consent from the patients to contact their rheumatologist to gather information on this subject.

Other reasons for discontinuation included maternal and child related reasons. Besides restart of medication, most reasons for cessation in this study were comparable with the general population[23]. Work related discontinuation of breastfeeding was reported in 7.7% of the patients in this study compared with 13.9% in the general population(p-value=0.05)[23]. The most likely explanation for this difference is the lower proportion of paid employment in RA patients[24, 25].

Higher HAQ in third trimester, presence of autoantibodies, and maternal smoking were significantly associated with discontinuation of breastfeeding < 12 weeks. It is conceivable that the HAQ and autoantibody status is related with severity of RA. In our study population, patients with higher HAQ and patients who were autoantibody positive, had higher disease activity postpartum and were more likely to restart MTX, leflunomide and biologicals at 6 or 12 weeks postpartum. It makes therefore sense to conclude that both a high HAQ as well as autoantibody positivity identify patients that have higher burden of disease and therefore are more likely to require additional medication postpartum, prohibiting them from breastfeeding. In addition, since the HAQ is a measure of functional status[26] it is likely that patients with higher HAQ discontinue breastfeeding due to functional impairment, either due to the physical difficulties associated with breastfeeding, or due to requirement of strong antirheumatic medications.

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Furthermore, maternal smoking was associated with early cessation of breastfeeding. Smoking was not related to medication use or disease activity postpartum. It is known that women with lower SES are more likely to smoke during and after pregnancy, and less likely to breastfeed their offsprings[27-31]. Although breastmilk loses many of its health promoting properties when the mother smokes, smoking mothers are advised not to discontinue breastfeeding[32]. Unfortunately, in our study the number of smoking mothers was too small to study associations with SES. In addition, SES was included in the multivariable model, and maternal smoking was independently associated with discontinuation of breastfeeding within 12 weeks, regardless of SES. In our reference population, there was no data on smoking or SES, therefore we could not make a comparison with our reference group.

In addition, RA patients with offsprings with low birth weight also require additional awareness. It has been shown earlier that preterm born infants with(very) low birth weight benefit the most from breastmilk[5]. In our study cohort, 85% of the mothers with an offspring with a birthweight<2500g discontinued breastfeeding<6 weeks postpartum, while the mean DAS28-CRP(3) postpartum was comparable in both birthweight-groups(data not shown). Approximately half of the patients with an offspring<2500g reported discontinuation due to restart of medication. According to the guidelines at the time this study was performed, sulfasalazine was considered not compatible with lactation in ill, stressed or premature infants[13, 14]. However, in that respect, patients receiving prednisone, hydroxychloroquine and non-selective NSAIDs could have continued breastfeeding. In our reference population, there was no data on low birthweight infants, therefore we could not compare our data with the reference group. Limited publications on breastfeeding in low birth weight infants are

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available. In the Netherlands(2000-2003), 50% of the infants with a birthweight ≤3000g were breastfed at 4 weeks postpartum[23], compared with 38% in our study population(p-value=0.06). Outside the Netherlands, the results were not consistent. Some studies report similar numbers of lactation in low birth weight infants[33, 34] compared with healthy infants, while others[35, 36] report lower numbers.

Another interesting finding from our study worth to mention is that, the DAS28-CRP(3) postpartum was significantly lower in breastfeeding patients compared with non-breastfeeding patients, despite taking less medication(when divided in breastfeeding and non-breastfeeding patients at every single time-point). This seems in contrast to the results of a previous study[1] that reported that first-time breastfeeding(but not breastfeeding after subsequent pregnancies) was associated with significantly more increase in RA disease activity postpartum compared with non-breastfeeders. In that study, the change in disease activity from third trimester to 6 months postpartum was compared and breastfeeding was defined as lactating for ≥4 weeks. When a similar analysis was performed in our study, no such association between first-time breastfeeding and an increase of RA disease activity could be observed(data not shown). That we could not reproduce the data of that study might also be related to the fact that that study was performed in a different time period, in which one was more reluctant to treat pregnant and lactating women. In addition disease activity was assessed with different methods. Although women with less severe disease are more likely to start and continue breastfeeding, the results of our study do not support the hypothesis that breastfeeding itself causes an increase in RA disease activity[1], e.g. by inducing high levels of prolactin.

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The results of this study will help to develop intervention strategies to support RA patients who wish to breastfeed. First of all, since a large proportion of RA patients do not start or continue breastfeeding for taking medication that in fact is compatible, education on medication use during lactation may be valuable for patients and their doctors. Not only rheumatologists, but also specialized nurses, midwives, and lactation consultants should be trained to increase their knowledge on this subject. In addition, access to up-to date medication resources for patients and their clinicians(e.g. evidence based online databases) are required.

Other patient groups that may benefit from targeted breastfeeding support include, patients with offsprings with low birth weight, and patients who smoke. Furthermore, since functional impairment might influence the start and duration of breastfeeding, ergonomic recommendations should be provided especially to patients with high HAQ.

In addition, the results of this study clearly show that a substantial number of patients do not breastfeed because they are in need of medication that is considered not compatible with breastfeeding. In this respect it is important to realize that guidelines on antirheumatic drug prescription during lactation are often not based on proven side-effects or toxicity for the offspring, but based on lack of safety data of those drugs, especially on transfer of medication into breastmilk[13]. This holds true for many medications, including methotrexate, one of the “cornerstones” of RA-treatment. In this respect the authors want to advocate that more research into his particular field is undertaken. That such research, although difficult to perform, is feasible, is shown by a recent study on the lack of transfer of certolizumab into breastmilk[37].

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This study has some limitations. Firstly, it was conducted approximately 10-16 years ago, and in time antirheumatic medication prescriptions have changed. However, we identified that there is a large group of patients that discontinue breastfeeding unnecessarily while using compatible antirheumatic drugs. This might reflect a lack of knowledge on this subject. It is questionable if the knowledge of doctors and nurses on this specific subject, and education of patients in the clinical practice has improved. Nevertheless, it would be interesting to perform a similar study on breastfeeding by RA-patients in this era of biologic therapies.

Secondly, in total, 33 women participated more than once in this study. To exclude possible selection bias in the obtained results, we performed a subgroup analysis, including only the first participation of the patients, and found comparable results.

In conclusion, our study demonstrates that RA is associated with lower proportions of women breastfeeding their offspring and earlier cessation compared with the general population. A considerable amount of patients discontinue breastfeeding(unnecessarily) so that they could start medication, despite the fact that many of the medications are considered safe to use during lactation. Given the known benefits of breastfeeding on the offspring, more effort in education in the clinical practice and more research into the transfer of medication into breastmilk might enable more RA patients to breastfeed.

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Table 1. Descriptive statistics of study population.*

	Baseline characteristics (n=249 pregnancies)
Maternal age at delivery, mean (sd) years	32.8 (3.8)
Duration RA at baseline, median (IQR) years	4.9 (2.2 – 9.8)
DAS28 3rd trimester, mean (sd)	3.4 (1.1)
3rd trimester DAS28-CRP#	
<2.6 (remission)	72 (28.9)
≥2.6 to <3.2 (low disease activity)	43 (17.2)
≥3.2 to ≤5.1 (intermediate disease activity)	118 (47.4)
>5.1 (high disease activity	16 (6.4)
HAQ in 3rd trimester, median (IQR)	0.75 (0.25 – 1.25)
Parity	
Nulliparous (no previous offsprings)	124 (51.5)
Multiparous (≥1 previous offspring)	117 (48.5)
RA-associated autoantibodies	
Either RF or ACPA positive, or both positive	186 (74.7)
Both negative	63 (25.3)
RF positive	172 (69.1)
ACPA positive	153 (61.5)
Presence of erosions	150 (60.2)
Methotrexate use in the past	143 (57.4)
Biological agent use in the past	44 (17.7)
Medication use during 3rd trimester	
Prednisone only	63 (25.3)
Sulfasalazine only	37 (14.9)
Both prednisone and sulfasalazine	22 (8.8)
Hydroxychloroquine (either alone or in combination)	4 (1.6)

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No medication during 3rd trimester	123 (49.4)
SES based on educational level	
Low	16 (6.4)
Middle	79 (31.7)
High	131 (52.6)
Unknown	23 (9.2)
Smoking$	22 (8.8)

*Values are number (%) unless indicated otherwise. Normally distributed data is presented with mean (sd), not normally distributed data is presented with median (IQR). RA= rheumatoid arthritis; IQR= interquartile range; RF= rheumatoid factor; ACPA= anti-citrullinated protein antibody; DAS28-CRP(3)= disease activity score in 28 joints using C-reactive protein levels.

Disease activity groups are defined according to the European League Against Rheumatism criteria. $ Smoking periconceptional or during pregnancy

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Table 2. Numbers and percentages of breastfeeding women 4-6 weeks, 12 weeks and 26 weeks postpartum in the PARA study and in the general population (Netherlands, 2005 [17])*.

	RA, PARA study (n=249)			General population (n=3009)		
	Total	**Exclusive**	**Partial**	**Total**	**Exclusive**	**Partial**
4-6 weeks	108 (43)#	91 (36)	17 (7)	1896 (63)#	1625 (54)	271 (9)
12 weeks	65 (26)#	47 (19)	18 (7)	1384 (46)#	1053 (35)	331 (11)
26 weeks	23 (9)#	11 (4)	12 (5)	1233 (41)#	752 (25)	481 (16)

*Values are number (%) unless indicated otherwise. # p-value <0.001 between RA and general population

RA= rheumatoid arthritis

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Table 3. Reasons for discontinuation of breastfeeding reported by the patients*.

	Discontinuation < 6 weeks postpartum (n=141)	Discontinuation 6 - 12 weeks postpartum (n=43)	Discontinuation 12 - 26 weeks postpartum (n=39)	Total (n=223)
Restart of medication				
- Total	86 (61.0)	28 (65.1)	15 (38.5)	129 (57.8)
- Not compatible	51	17	8	76
- Compatible	35	11	7	53
Maternal reasons	44 (31.2)	14 (32.6)	19 (48.7)	77 (34.5)
- no desire to	15	.	1	16
- not enough milk	13	8	12	33
- work related	.	4	3	7
- too much effort	7	.	2	9
- mastitis	4	1	.	5
- breast surgery	3	.	.	3
- unknown	.	1	1	2
Child related reasons	11 (7.8)	1 (2.3)	3 (7.7)	15 (6.7)
- struggle to latch	6	.	1	7
- failure to thrive	4	1	1	6
- illness	1	.	1	2
Combination of maternal and child related reasons	.	.	1 (2.6)	1 (0.4)
- unknown	.	.	1	1
Unknown	.	.	1 (2.6)	1 (0.4)

*Values are number (%) unless indicated otherwise.

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Table 4. Disease activity and medication use postpartum*.

	DAS28-CRP(3)	Prednisone	SSZ	HCQ	Non-selective NSAIDs	MTX#	Leflunomide#	TNF inhibitors#	Selective COX II inhibitors#	Azathioprine#
Breastfeeding										
6 weeks (n=108)	3.1	21 (19.4)	23 (21.3)	0 (0)	4 (3.7)	0 (0)	0 (0)	1 (0.9)	0 (0)	3 (2.8)
12 weeks (n=65)	3.4	15 (23.1)	17 (26.2)	0 (0)	9 (13.8)	0 (0)	0 (0)	1 (1.5)	1 (1.5)	3 (4,6)
26 weeks (n=23)	3.0	3 (13.0)	7 (30.4)	0 (0)	4 (17.4)	0 (0)	0 (0)	0 (0)	0 (0)	3 (13.0)
Non-breastfeeding										
6 weeks (n=141)	3.5	65 (46.1)	42 (29.8)	10 (7.1)	37 (26.2)	46 (32.6)	0 (0)	12 (8.5)	8 (5.7)	3 (2.1)
12 weeks (n=184)	3.7	75 (40.8)	57 (31.0)	19 (10.3)	60 (32.6)	76 (41.3)	3 (1.6)	23 (12.5)	15 (8.2)	3 (1.6)
26 weeks (n=220)	3.5	75 (34.1)	63 (28.6)	18 (8.2)	64 (29.1)	92 (41.8)	4 (1.8)	29 (13.2)	16 (7.3)	2 (0.9)

* Values are number (%) unless indicated otherwise. # considered not compatible with lactation at the time this study was conducted SSZ= sulfasalazine; HCQ= hydroxychloroquine; NSAIDs= Nonsteroidal anti-inflammatory drugs; MTX= methotrexate; TNF= tumor necrosis factor

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Table 5. 3rd trimester factors associated with discontinuation of breastfeeding < 12 weeks

	Discontinuation of breastfeeding < 12 weeks #			
	Univariable		Multivariable$ (n=226)	
	OR	P- value	OR	P- value
HAQ 3rd trimester ≥0.75	3.121+	<0.001+	3.669*	<0.001*
Autoantibody status positive	2.649+	0.002+	3.210*	0.003*
Smoking%	3.841+	0.075+	5.902*	0.032*
MTX use in past	1.857+	0.034+	1.659	0.143
SES based on educational level	0.696+	0.156+	0.661	0.150
Prednisone use 3rd trimester	3.378+	0.001+	1.924	0.114
Presence of erosions	1.693+	0.071+	-	-
DAS28-CRP(3) 3rd trimester	1.305+	0.052+	-	-
Sulfasalazine use 3rd trimester	0.991	0.980		
VAS GH	0.999	0.474		
Maternal age	0.989	0.774		
Parity ≥ 1	1.106	0.737		

OR= Odds Ratio; HAQ= Health Assessment Questionnaire; MTX= methotrexate; SES= socioeconomic status; DAS28-CRP(3)= Disease Activity Score in 28 joints using C-reactive protein levels ; VAS GH= Visual Analogue Score Global Health. # Based on logistic regression $ Multivariable model after forward selection (limit for inclusion: P < 0.20) and backward selection (limit for exclusion: P ≥ 0.20) % smoking periconceptional or during pregnancy, + Variables taken forward if p <0.20, * Statistically significant in the multivariable model

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