

A Population-level Analysis of the Differing Effects of Rheumatoid Arthritis and Spondyloarthritis on Peripartum Outcomes

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ABSTRACT. Objective. The effects of rheumatoid arthritis (RA) and spondyloarthritis (SpA) on maternal and neonatal outcomes at a population level have not previously been well compared.

Methods. A contemporary pregnancy cohort of 312,081 women and corresponding birth events was assembled for the province of Alberta from the random selection of 1 live birth event per woman. We identified 3 groups: (1) no inflammatory arthritis (no IA, n = 308,989), (2) RA (n = 631), and (3) SpA (n = 2461). We compared maternal and neonatal outcomes, comorbid conditions, and medication use among the 3 groups. Multivariable logistic regression models evaluated the independent association between RA and SpA, relative to no IA, and the outcomes of small for gestation age (SGA) and hypertensive disorders during pregnancy.

Results. Pregnant women with RA were significantly more likely to have preterm delivery (13.5%), cesarean delivery (33.9%), hypertensive disorders in pregnancy (10.5%), and SGA babies (15.6%), compared to pregnant women with either SpA or no IA. Nonsteroidal antiinflammatory drugs and corticosteroid use were significantly higher in pregnant women with RA compared to the other groups. Women with RA were significantly more likely to have an SGA baby (OR 1.51, 95% CI 1.21–1.88; $p < 0.01$), and hypertensive disorder in pregnancy (OR 1.51, 95% CI 1.16–1.97; $p < 0.01$), compared to women with no IA, while no difference was found between women with SpA and those with no IA.

Conclusion. Women with RA have a higher risk of worse maternal and neonatal outcomes, whereas the risk of these events is similar between women with and without SpA. (J Rheumatol First Release August 15 2019; doi:10.3899/jrheum.181320)

Key Indexing Terms:

RHEUMATOID ARTHRITIS

SPONDYLOARTHRITIS

PERIPARTUM OUTCOMES

Rheumatoid arthritis (RA) and spondyloarthritis (SpA) are the 2 most common types of inflammatory arthritis (IA) to affect women of child-bearing age. It is estimated that about 0.5 to 1% of adults have RA¹. The overall prevalence of SpA, including axial and peripheral subsets as well as psoriatic, reactive, and enteropathic forms, varies by study methodologies and geographic areas, ranging from 1.35% in North America and 0.54% in Europe to 0.22% in South Asia². The prevalence of specific subsets of SpA depends also upon

criteria used to define the disease and the genetic background of the population studied, with rates for ankylosing spondylitis (AS) ranging from 0.52 to 0.55% and axial SpA (axSpA) from 1.0 to 1.4%^{3,4}.

While affecting women of child-bearing age, the potential effect of these 2 types of IA on peripartum outcomes is not commonly compared at the population level. Although inflammation is the hallmark of both types of arthritis, significant differences in pathophysiology, disease course, and effective therapeutics may translate into differing effects on maternal and neonatal outcomes^{2,5,6,7}. Currently, the most consistently reported adverse peripartum outcomes for RA include low-birthweight babies, maternal preeclampsia, and cesarean delivery^{8,9,10,11}. In contrast, the effect of SpA on peripartum outcomes is less clear^{12,13,14,15,16,17,18}. Another consideration for both types of IA include medication use during pregnancy. Medications such as corticosteroids and nonsteroidal antiinflammatory drugs (NSAID) may worsen peripartum outcomes^{19,20}. Alternatively, the increased use of tumor necrosis factor (TNF) inhibitors may reduce disease activity, and therefore reduce the risk for worse peripartum outcomes^{21,22,23,24}.

The objective of our study was to compare maternal and

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neonatal outcomes among women with RA, SpA, and those without IA in a large, population-based cohort of pregnant women with universal health coverage. We also examined the frequency of use of various medications during pregnancy among the 3 groups.

MATERIALS AND METHODS

Data sources and linkage. Our study is based on data from the Alberta Pregnancy-Birth cohort, which has been previously described²⁵. Having at least 4.08 million people since 2011, Alberta is the fourth most populous province in Canada, with high birthrates, immigration, and interprovincial migration, and noteworthy racial and ethnic composition (80% white, 14% visible minority, and 6% aboriginal)²⁶. In brief, the Alberta cohort was developed by using a unique scrambled patient identifier to link the following data for mothers and their offspring:

- (1) Detailed birth information, including birth weight, gestational age, and parity, from the Alberta Vital Statistics–Birth Database.
- (2) Hospitalization records from the Discharge Abstract Database.
- (3) Outpatient records, including emergency department visits, from the Ambulatory Care Classification System database.
- (4) Physician office visit records from the practitioners claims database.
- (5) Demographic information including age, sex, ethnicity (based on validated naming algorithms)^{27,28,29}, and geographic residence from the Alberta Health Care Insurance Population registry.
- (6) Pharmaceutical claim records from the Pharmaceutical Information Network database.
- (7) Mortality data from the Vital Statistics–Death Database.

In addition, we linked the 2011 National Household Survey from Statistics Canada, which includes information on annual median household income at the neighborhood level as a measure of socioeconomic status. Ethics approval for this study was obtained from the University of Alberta Institutional Review Board (Pro00056999).

Study design and population. Our patient population consisted of all live singleton births that occurred between January 1, 2005, and December 31, 2014. Women who were older than 54 years at the time of delivery as previously described²⁵ or who were not residents of Alberta during the entire course of the pregnancy were excluded from the analysis. The unit of analysis was the woman, and for women with multiple birth events during the study time period, 1 event was randomly selected. Women were categorized into 3 groups: RA, SpA, and no IA. Based on the previous work of diagnostic algorithms for case ascertainment of RA and SpA, we identified women with RA or SpA as those having either of the following prior to the delivery date: (1) one hospitalization or (2) two outpatient records or physician office visits (including emergency department and specialized clinic visits) within a 2-year period that were at least 2 months apart, with a World Health Organization International Classification of Diseases (ICD) version 9 and 10 code for the disease^{30,31,32}. RA or SpA diagnoses could have been made by any type of physician including family physicians or specialists. The following previously validated codes were used for RA: ICD-9: 714.0, 714.3; ICD-10: M05, M06, M08. These were used for SpA (spondyloarthritis/AS): ICD-9: 720; ICD-10: M45–M49, M08.1; SpA (psoriasis): ICD-9: 696; ICD-10: L40.0–L40.4, L40.8, L40.9, and SpA [psoriatic arthritis (PsA)]: ICD-9: 696; ICD-10: L40.5. If both RA and SpA diagnoses were identified by this algorithm, the woman was considered an RA case.

Health conditions. The presence of other chronic health conditions [i.e., hypertension (HTN), renal disease, ischemic heart disease, cerebrovascular disease, heart failure, and thyroidism] was identified based on their presence either during the delivery or hospitalization, or a prior hospitalization that occurred between 1997 and the delivery date. Preexisting diabetes and gestational diabetes were identified using hospitalization, outpatient, and physician claims records^{33,34}.

Outcomes. Our primary outcomes of interest were rates of small for gesta-

tional age (SGA) infants (defined as under 10th percentile birth weight) and hypertensive disorders in pregnancy (i.e., preexisting HTN, preeclampsia, eclampsia, and gestational HTN complicating current pregnancy, defined by ICD-10 codes I10–I15, O11, O13, O14, or O15, in any diagnosis field of hospital admissions, within 270 days prior to delivery)³⁵. Secondary maternal and neonatal outcomes of interest included the following: maternal cesarean delivery (emergent and elective), induction (as recorded during birth hospitalization), preterm delivery, mortality within 40 days of birth (Vital Death Database), gestational diabetes; neonatal birth weight, large for gestational age (defined as over 90th percentile birth weight), death within 30 days of delivery, congenital anomalies, and number of days the baby spent in neonatal intensive care unit (NICU) during the birth hospitalization (inpatient database). Newborn congenital anomalies were identified in all diagnosis fields of hospitalizations, emergency department, and outpatient clinic visits at the time and after birth. For birth events after January 1, 2009, we examined the use of specific medications using the Anatomical Therapeutic Chemical Classification System during the 270 days prior to delivery.

Statistical analysis. Maternal characteristics (demographics and chronic health conditions) at time of delivery, maternal and neonatal outcomes, and medication use during the 270 days prior to delivery were compared across the 3 groups (RA, SpA, and no IA). Categorical variables were compared using chi-square tests and continuous variables were compared using 1-way ANOVA. Multivariable logistic regression models were used to examine the independent association between IA type (RA and SpA relative to no IA) and the primary outcomes of interest. Other variables included in the models were maternal age at delivery (per 5 yrs), rural residence (urban vs rural), ethnicity (general population excluding Chinese, South Asian, Status Aboriginal; and Chinese, South Asian, Status Aboriginal), 2010 annual household income at forward sortation area level per \$10,000, nulliparity (yes/no), and presence of renal disease, HTN, hypertensive disorders in pregnancy (controlled for only in the analysis of SGA), diabetes, gestational diabetes, cerebrovascular disease, ischemic heart disease, and hyper- and hypothyroidism (all yes/no). OR were used to examine the association between each medication category and the outcomes of interest in the entire cohort.

RESULTS

Between January 1, 2005, and December 31, 2014, there were 487,938 live births from 321,080 women in Alberta, Canada. This resulted in 473,899 births being retained for the analysis, after excluding nonresidents (n = 5664), mothers who did not meet the age criteria (n = 36), non-singleton births (n = 8164), and records with missing or incorrect data (n = 144). One live birth event per woman was randomly selected, resulting in a final cohort of 312,081 women. Of these, 631 (0.2%) women had RA, 2461 (0.8%) had SpA, and 308,989 (99%) had no IA. Women without IA had a slightly lower mean (SD) age at delivery [29.3 (8.4) yrs] and formed a slightly larger proportion of Chinese (3.8%) and South Asian women (3.2%; p < 0.01 for all; Table 1). Women with RA had the highest proportion of Status Aboriginal patients (11.7%) and the highest rates of cerebrovascular (0.5%) and thyroid disease (9.0%; p < 0.01 for all; Table 1). Women with RA and SpA were more likely to live in a rural area at the time of delivery, and had higher rates of HTN and diabetes compared to those without IA.

Overall, pregnant women with RA had worse maternal and neonatal outcomes than those with SpA or no IA (Table 2). Specifically, pregnant women with RA were significantly

Table 1. Baseline characteristics for 312,081 pregnant women in Alberta from January 1, 2005, to December 31, 2014.

Characteristics	No IA	RA	SpA*	p
Women, n	308,989	631	2461	
Age at delivery, yrs, mean (SD)	29.3 (8.4)	30.4 (5.6)	30.5 (20.3)	< 0.01
Rural residence at delivery	45,691 (14.8)	119 (18.9)	407 (16.5)	< 0.01
Ethnicity				
General population	270,079 (87.4)	530 (84.0)	2257 (91.7)	< 0.01
Chinese	11,667 (3.8)	9 (1.4)	45 (1.8)	
South Asian	9844 (3.2)	18 (2.9)	33 (1.3)	
Status Aboriginal	17,399 (5.6)	74 (11.7)	126 (5.1)	
2010 annual household income, Can\$, mean (SD)	83,022 (24,333)	81,806 (22,464)	84,041 (23,789)	0.05
Nulliparous	147,931 (47.9)	293 (46.4)	1130 (45.9)	0.12
Renal disease	161 (0.1)	2 (0.3)	3 (0.1)	< 0.01
Hypertension	527 (0.2)	5 (0.8)*	10 (0.4)	< 0.01
Diabetes	2966 (1.0)	14 (2.2)*	37 (1.5)	< 0.01
Cerebrovascular disease	273 (0.1)	3 (0.5)	1 (0.0)	< 0.01
Ischemic heart disease	77 (0.0)	1 (0.2)	1 (0.0)	< 0.01
Thyroid disease	12,043 (3.9)	57 (9.0)	148 (6.0)	< 0.01

Data are n (%) unless otherwise indicated. * Includes SpA, ankylosing spondylitis, psoriasis, and psoriatic arthritis. IA: inflammatory arthritis; RA: rheumatoid arthritis; SpA: spondyloarthritis.

Table 2. Maternal and neonatal outcomes for 312,081 pregnant women in Alberta from January 1, 2005, to December 31, 2014.*

Characteristics	No IA	RA	SpA**	p
Preterm delivery	21,997 (7.1)	85 (13.5)	181 (7.4)	< 0.01
Cesarean delivery	87,771 (28.4)	214 (33.9)	715 (29.1)	< 0.01
Elective cesarean delivery	37,053 (12.0)	95 (15.1)	338 (13.7)	< 0.01
Emergent cesarean delivery	50,718 (16.4)	119 (18.9)	377 (15.3)	0.09
Induction	82,415 (26.7)	182 (28.8)	722 (29.3)	< 0.01
Mortality within 40 days of birth	17 (0.0)	0 (0.0)	1 (0.0)	0.07
Hypertensive disorders in pregnancy***	19,831 (6.4)	66 (10.5)	179 (7.3)	< 0.01
Gestational diabetes	18,595 (6.0)	32 (5.1)	162 (6.6)	0.3
Birth weight, g, mean (SD)	3349 (562)	3224 (597)	3364 (548)	< 0.01
Small for gestational age	34,757 (11.3)	98 (15.6)	260 (10.6)	< 0.01
Large for gestational age	27,706 (9.0)	62 (9.8)	238 (9.7)	0.36
Neonatal death within 30 days of birth	973 (0.3)	3 (0.5)	11 (0.4)	0.39
Congenital anomaly	5751 (1.9)	18 (2.9)	52 (2.1)	0.12
Mean (SD) days in NICU	0.8 (5.0)	1.2 (5.7)	0.8 (4.5)	0.14

Data are n (%) unless otherwise indicated. * Sensitivity analyses evaluating maternal and neonatal outcomes in primiparous women revealed similar results. ** Includes SpA, ankylosing spondylitis, psoriasis, and psoriatic arthritis. *** Includes gestational hypertension, preeclampsia, and eclampsia. IA: inflammatory arthritis; RA: rheumatoid arthritis; SpA: spondyloarthritis; NICU: neonatal intensive care unit.

more likely to have preterm deliveries (13.5%), an elective or emergent cesarean delivery (33.9%), hypertensive disorders in pregnancy (10.5%), a baby with a lower mean (SD) birth weight [3224 g (597)], and an SGA baby (15.6%; $p < 0.01$ for all), compared to pregnant women with either SpA or no IA. Pregnant women with SpA had the highest induction rates (29.3%; $p < 0.01$; Table 2). Similar among all 3 groups were maternal and neonatal mortality, rates of infant congenital anomaly, and mean number of NICU days.

Women with RA were significantly more likely to use several different types of medications in the 270 days prior to delivery, such as steroids (15.1%), NSAID (11.4%), antimalarials (18.8%), disease-modifying antirheumatic drugs (DMARD; 7.9%), and biologic medications (8.4%;

$p < 0.0001$ for all; Table 3). NSAID use decreased across all groups from the first to third trimesters. Across the entire cohort ($n = 195,272$), the use of steroids, NSAID, and biologics was associated with higher odds of hypertensive disorders of pregnancy, while antimalarials were associated with higher risk of an SGA infant (Appendix 1).

In multivariate analyses, women with RA were significantly more likely to have an SGA baby (OR 1.51, 95% CI 1.21–1.88; $p < 0.01$) and a hypertensive disorder in pregnancy (such as gestational HTN, preeclampsia, or eclampsia; OR 1.51, 95% CI 1.16–1.97; $p < 0.01$), compared to women without IA (Figure 1). There was no difference between women with SpA and those without IA for SGA (OR 0.97, 95% CI 0.85–1.10; $p = 0.64$) or hypertensive disorders

Table 3. Medication use during the 270 days prior to delivery among 195,272 pregnant women in Alberta, from January 1, 2009, to December 31, 2014.

Medications	No IA, n = 193,242	RA, n = 430	SpA, n = 1600*	p
Corticosteroids (prednisone)	1175 (0.6)	65 (15.1)	22 (1.4)	< 0.0001
NSAID	3023 (1.6)	49 (11.4)	41 (2.6)	< 0.0001
First trimester	2401 (1.2)	39 (9.1)	28 (1.8)	
Second trimester	464 (0.2)	18 (4.2)	11 (0.7)	
Third trimester	347 (0.2)	4 (0.9)	8 (0.5)	
Antimalarials	160 (0.1)	81 (18.8)	5 (0.3)	< 0.0001
DMARD**	42 (0.0)	34 (7.9)	6 (0.4)	< 0.0001
Total biologic medications	114 (0.1)	36 (8.4)	27 (1.7)	< 0.0001
Etanercept (TNFi)	1 (0.0)	18 (4.2)	6 (0.4)	
Infliximab (TNFi)	67 (0.0)	5 (1.2)	8 (0.5)	
Adalimumab (TNFi)	46 (0.0)	6 (1.4)	12 (0.8)	
Certolizumab (TNFi)	0 (0.0)	3 (0.7)	0 (0.0)	
Golimumab (TNFi)	0 (0.0)	1 (0.2)	1 (0.1)	
Abatacept (T cell costimulation inhibitor)	0 (0.0)	0 (0.0)	0 (0.0)	
Rituximab (B cell depletory)	0 (0.0)	0 (0.0)	0 (0.0)	
Tocilizumab (IL-6 receptor blocker)	0 (0.0)	3 (0.7)	0 (0.0)	

All data except p values are n (%). * SpA, ankylosing spondylitis, psoriasis, and psoriatic arthritis. TNFi: tumor necrosis factor inhibitors; **DMARD: disease-modifying antirheumatic drugs including sulfasalazine, cyclosporine, and sodium aurothiomalate; IA: inflammatory arthritis; RA: rheumatoid arthritis; SpA: spondyloarthritis; NSAID: nonsteroidal antiinflammatory drugs; IL: interleukin.

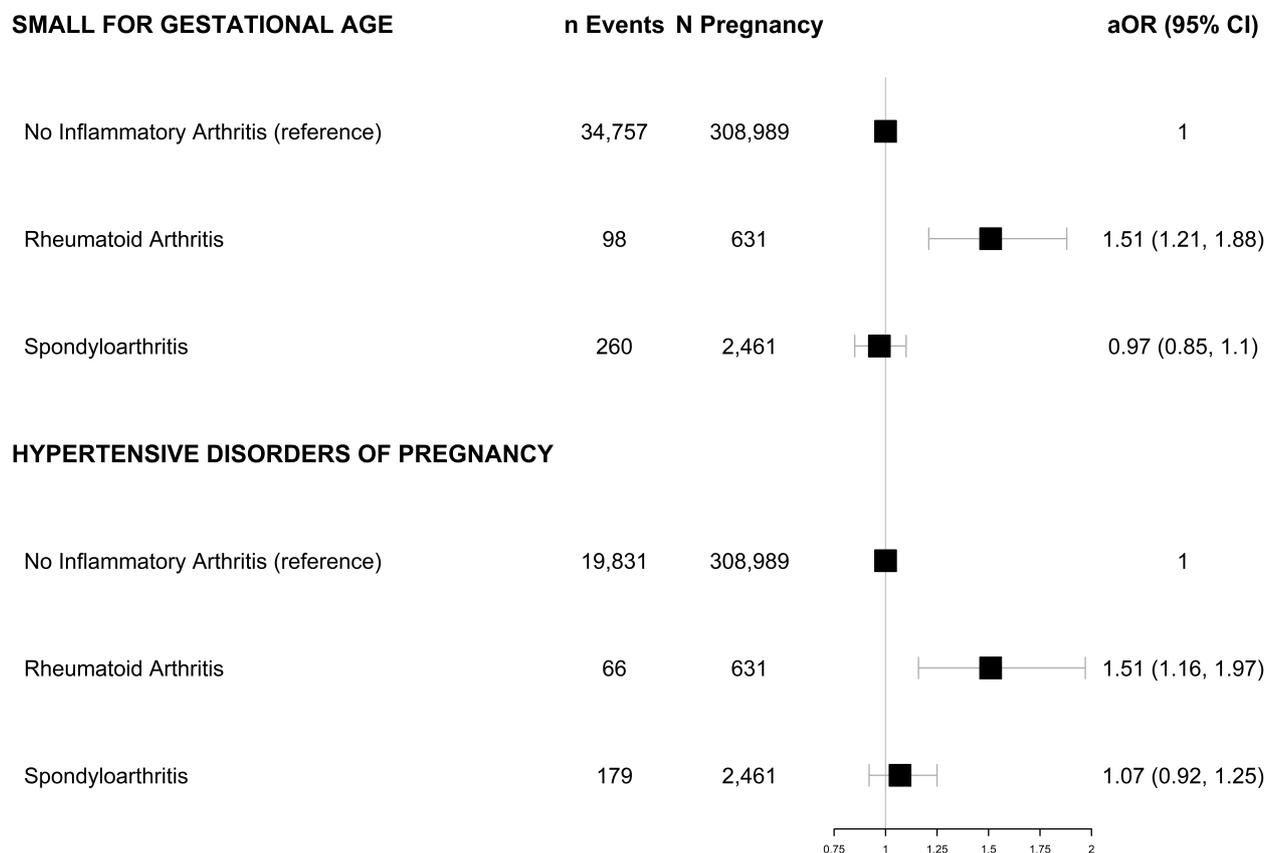


Figure 1. Forest plot for the association between inflammatory arthritis and the outcomes of small for gestational age and hypertensive disorders in pregnancy. Spondyloarthritis group includes spondyloarthritis, ankylosing spondylitis, psoriasis, and psoriatic arthritis. Hypertensive disorders in pregnancy include gestational hypertension, preeclampsia, eclampsia, and preexisting hypertension complicating current pregnancy. Adjusted (aOR) for the following: age at delivery, rural residence, ethnicity, 2010 annual household income, nulliparity, renal disease, hypertension, hypertensive disorders in pregnancy, diabetes, gestational diabetes, cerebrovascular disease, ischemic heart disease, and hyper/hypothyroidism.

in pregnancy (OR 1.07, 95% CI 0.92–1.25; $p = 0.39$). The association between other factors included in the multivariable model and outcomes is provided in Figure 1. Sensitivity analyses evaluating subtypes of SpA including psoriasis/PsA and AS/SpA did not significantly change the maternal and neonatal outcome results (data not shown).

DISCUSSION

To our knowledge, this is the first comparative population-based cohort study evaluating the effect of RA and SpA compared to no IA on peripartum outcomes. We confirmed findings of previous studies in which women with RA were more likely to have SGA babies and hypertensive disorders in pregnancy, such as preeclampsia, compared to women with no IA. This is in contrast to the findings for the SpA group, whereby the majority of maternal and neonatal outcomes were less prevalent than in RA and generally not significantly different from the no IA population. Interestingly, rates of induction in women with SpA were slightly greater than in those with RA or no IA, which is not previously reported. Possible explanations include the combined effect of the evolving pregnancy-related back pain superimposed on inflammatory back pain and/or possible presence of hip disease in women with SpA compared to those with RA or without IA. The rates of preterm birth and SGA births in the no IA and SpA populations were similar to those seen between 1997 and 2004 as part of 2006 Alberta vital statistics data in which preterm birth rates were 8.3% and SGA rates in singleton births were 8.0%³⁶.

Our results are similar to previous findings among patients with RA of smaller babies, more cesarean deliveries, preterm labor, and hypertensive disorders such as preeclampsia^{8,9,11}. In our study, more women with RA delivered in rural locations and were of indigenous status, compared to the SpA and no IA groups. Recent work from the Canadian Early Arthritis Cohort identified worse outcomes in aboriginal versus white patients with RA despite similar management strategies, suggesting a complicated interplay between possible biologic differences and healthcare inequities³⁷. The contribution of these differences to the worse maternal and neonatal outcomes and comorbidities, including diabetes and HTN, were adjusted for in the multivariate analyses.

Multiple comorbidities were worse for pregnant women with RA than for the other 2 groups, including renal disease, HTN, diabetes, cerebrovascular disease, ischemic heart disease, and thyroid disease, which are also well recognized as more prevalent in general RA cohorts^{38,39,40,41,42,43,44}. Although our finding of no significant effect of SpA on maternal and neonatal outcomes is similar to a systematic literature review focused on peripartum outcomes in women with psoriasis⁴⁵, it differs from the recent population-based study from Denmark and Sweden that found greater risk of gestational diabetes, gestational HTN, preeclampsia, and elective and emergency cesarean deliveries in women with

psoriasis and PsA⁴⁶. These contradictory findings suggest the need for further studies examining these issues.

Women with RA were statistically more likely to have filled at least 1 prescription for NSAID and corticosteroids in the 270 days prior to delivery than women with SpA, followed by the non-IA group. Despite the benefits of NSAID for both RA and SpA, the progressively lower use of NSAID over each trimester per group was expected, given the association of premature closure of the ductus arteriosus because of the inhibition of prostaglandin synthesis in the third trimester with multiple complications, such as pulmonary HTN and fetal death^{20,21,22,23}. The increased use of corticosteroids in RA, compared to SpA, likely reflected the known reduced efficacy of corticosteroids in axSpA and clinical experience of rebound psoriasis flares related to tapering corticosteroids^{47,48}. Moreover, the greater rates of NSAID, DMARD, and biologic use in women with RA versus SpA indirectly suggests greater disease activity in women with RA compared to SpA during pregnancy, which may worsen peripartum outcomes in women with RA. Further extrapolation is inappropriate given the overall low use of medications and the impossibility of accounting for disease activity in this cohort.

While perceived as rescue therapy for RA in pregnancy, corticosteroid use in all pregnant patients has been associated with multiple adverse peripartum events, including premature rupture of membranes, intrauterine growth retardation, pregnancy-induced HTN, and gestational diabetes²³. Despite reported safety in pregnancy, the actual use of antimalarials in pregnancy was lower than expected for RA, but was as expected in SpA, given the roles of antimalarials in flaring psoriasis and having no efficacy in axSpA⁴⁸. TNF inhibitors were prescribed the most of all biologic medications for both RA and SpA, likely because of their increasingly recognized safety in the peripartum period and known efficacy for RA and SpA^{23,49}. The overall low rates of TNF inhibitor use for both RA and SpA may be attributable to the evolving understanding of the safety of TNF inhibitors in pregnancy during the study period as well as the differential uptake in treating RA and SpA. In the future, the number of TNF inhibitor prescriptions may surpass those for corticosteroids, given the potential effect on maternal and neonatal outcomes and relative safety profiles.

We acknowledge several limitations of our study. The estimation of pregnancy start date is indirect, having been estimated by calculating 270 days prior to delivery. Our study relies on the completeness and accuracy of coding for RA and SpA in the administrative healthcare databases. We did not validate our algorithm in a sample of medical records owing to feasibility issues. Rather, our case ascertainment was based on the work of others in RA and SpA, whereby algorithms including physician billings were found to have high sensitivity, with improved specificity and positive predicted value when multiple physician or specialist claims were made^{30,32}. The ICD-9 codes for psoriasis and PsA are

the same, which prevented further differentiation between the women with psoriasis and PsA and helps explain the larger total number of SpA versus RA mothers. This limitation was felt to be minor, because the underlying disease process of psoriasis for skin and joints is overall the same. In a sensitivity analysis, nearly identical results to the entire SpA group were found for maternal and neonatal outcomes, when women with psoriasis and PsA were analyzed separately. Despite recognized heterogeneity among patients with PsA and axSpA, the group was combined because of the common pathophysiologic and genetic bases of these diseases, as reflected in their grouping together by organizations such as the Assessment of the Spondyloarthritis international Society⁵⁰.

Several important confounders that may have affected our results were not available for analysis. These include laboratory data (e.g., serologies, genetic markers, and acute-phase reactants), IA disease activity, disease duration, education, and smoking. The change in the classification criteria for both RA and SpA in 2010 and 2011, respectively, with improved sensitivities and specificities, might have led to the inclusion of patients with earlier disease or other diagnoses in the last few years of the cohort, thus diluting the effect of disease activity on our results. However, the effect of newer criteria was felt to be negligible overall because diagnoses were made not only by rheumatologists but other physicians in situations where uptake of new criteria would be slow for the latter third of the cohort. Maternal weight was not available as a clinical covariate, which may be an important confounder in the relationship between IA and the outcomes of SGA and hypertensive disorders in pregnancy. Other than adjusting for parity, birth weight comparisons were crude because maternal smoking and body mass indices were not available. Interpretation of the effect of medications on peripartum outcomes of interest is limited because of small sample size and the inadequacy of the medication data. While the results are generalizable across Canada, the lower rates of African American and Hispanic ethnicities may limit the applicability to particular subgroups of RA and SpA in other countries.

The strengths associated with this study are notable. First, the data are based on a large contemporary, population-based sample of women giving birth in a defined geographic area, with universal healthcare access. Therefore, our study does not have the potentially appreciable selection bias that can occur in non-population-based studies. We also had information on a number of potentially important confounding demographic, maternal, and neonatal variables that we were able to control for in multivariate analyses. A sensitivity analysis of primiparous women confirmed similar findings for maternal and neonatal outcomes between women with RA, SpA, and no IA, acknowledging the important predictive factor of a first adverse pregnancy outcome on future pregnancies. The results are generalizable to the subgroups of RA and SpA given the generally diverse ethnic breakdown of Alberta.

While women with RA have a higher risk of worse

maternal and neonatal outcomes, the risk of these events in women with SpA is similar to those in women with no IA. This reflects potential differences between the underlying pathophysiology of these 2 different types of IA. Further work is required to understand the important effect of medication use, particularly corticosteroids and NSAID in this population, especially given the increasing uptake of a potentially safer category of medications, the TNF inhibitors.

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APPENDIX 1. Medication use and association with peripartum outcomes across the entire cohort (n = 195,272).

Characteristics	Steroids	NSAID	Antimalarials	DMARD	Biologics
Those taking medication, n (%)	1262 (0.6)	3113 (1.6)	246 (0.1)	82 (0.0)	177 (0.1)
Small for gestational age (OR, 95% CI)	1.17 (0.99–1.37)	0.92 (0.82–1.03)	1.89 (1.39–2.51)*	1.96 (1.16–3.16)*	1.34 (0.88–1.96)
Hypertensive disorders of pregnancy (OR, 95% CI)	1.47 (1.21–1.76)*	1.35 (1.19–1.53)*	1.36 (0.85–2.06)	1.50 (0.67–2.92)	2.06 (1.31–3.1)*

*p < 0.05. NSAID: nonsteroidal antiinflammatory drugs; DMARD: disease-modifying antirheumatic drug.