Reproductive patterns and maternal and pregnancy outcomes in women with psoriasis—A population-based study

Mats Lambe, MD, PhD,[a,b] Anna V. Bergstrom, MD,[c] Anna L. V. Johansson, PhD,[a] and Caroline E. Weibull, PhD[a,d]
Stockholm and Uppsala, Sweden

Background: Data on pregnancy outcomes in women with psoriasis are conflicting.

Objective: We examined whether maternal psoriasis affects the risk of adverse maternal and pregnancy outcomes.

Methods: We used population-based data to compare reproductive patterns in women with and without psoriasis. Odds ratios (ORs) with 95% confidence intervals (CIs) for adverse outcomes were estimated with adjustments for maternal age, period of childbirth, smoking, and prepregnancy body mass index.

Results: Compared with women without psoriasis, women with psoriasis were younger at first birth and had longer interpregnancy intervals but did not differ in final parity. Risk estimates in women with psoriasis were elevated for pregnancy hypertension (OR, 1.37; 95% CI, 1.19-1.58), premature rupture of membranes (OR, 1.15; 95% CI, 1.04-1.27), large for gestational age (OR, 1.11; 95% CI, 1.01-1.21), cleft palate (OR, 1.69; 95% CI, 1.07-2.66), and unspecified malformations (OR, 1.08; 95% CI, 1.01-1.16).

Limitations: No information was available on lifestyle, disease severity, or type and duration of treatment. Small numbers hampered the assessment of rare outcomes.

Conclusion: Although there was no evidence that fertility is negatively affected, women with psoriasis were at an increased risk of several adverse maternal and pregnancy outcomes. Our findings add to a growing body of evidence that pregnancies in women with psoriasis need special monitoring. (J Am Acad Dermatol 2020;82:1109-16.)

Key words: malformations; maternal outcomes; pregnancy outcomes; parity; psoriasis; register; Sweden.

Psoriasis is a common disease with an autoimmune-mediated etiology and a bimodal age of onset, with a first incidence peak in individuals who are 15 to 39 years old and a second peak in those 50 to 59 years old.[1] Hence, women of reproductive age with psoriasis represent a significant patient group. Annually, there are at least an estimated 65,000 births in the United States to women with psoriasis, approximately one fourth of whom have moderate to severe disease.[2]

It remains unknown whether psoriasis has an impact on fertility.[3] Also, although autoimmune diseases have been associated with an increased risk of adverse pregnancy outcomes such as preterm birth, small for gestational age, and congenital malformations in women with inflammatory bowel

From the Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm[a]; Regional Cancer Center, Uppsala University Hospital, Uppsala[b]; Dermatology Unit, Department of Medicine, University Hospital, Uppsala[c]; and Clinical Epidemiology Division, Department of Medicine Solna, Karolinska Institutet, Stockholm.[d]

Drs Weibull and Johansson contributed equally to this article.

Funding sources: Supported by an Investigator Initiated Research Grant from Pfizer Inc. (IIR WS2059711) and the Karolinska Institutet Research Funds. The sponsors had no role in the study design, data collection, data analysis, data interpretation or writing of the report.

Disclosure: Dr Lambe owns stocks in AstraZeneca and Pfizer Inc. Drs Bergstrom, Johansson, and Weibull have no conflicts of interest to declare.

Accepted for publication May 22, 2019.

Reprints not available from the authors.

Correspondence to: Mats Lambe, MD, PhD, Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, PO Box 281, 171 77 Stockholm, Sweden. E-mail: mats.lambe@ki.se.

Published online February 3, 2020.

0190-9622/$36.00

https://doi.org/10.1016/j.jaad.2019.05.099

disease,[4-6] data on pregnancy outcomes in women with psoriasis are conflicting. A systematic review of 9 observational studies concluded that although results have differed across the mostly small studies conducted to date, the collective evidence does not support an increased risk of adverse pregnancy outcomes in women with psoriasis. However, 4 of the included studies reported statistically significant increased risk of at least 1 adverse pregnancy outcome.[7] These inconsistences have highlighted a need to systematically record pregnancy data in women with psoriasis. However, attempts in the United States to establish a psoriasis and pregnancy register have been hampered by low enrollment.[2] A recent study based on combined data from population-based registers in Denmark and Sweden reported increased risk for several adverse outcomes in women with psoriasis, including gestational diabetes, gestational hypertension, pre-eclampsia, and cesarean birth.[8]

CAPSULE SUMMARY

- Our findings add to a growing body of evidence that the risk for some adverse maternal and pregnancy outcomes is elevated in women with psoriasis.
- Pregnancies in women with psoriasis may need special monitoring.

Based on information retrieved from Swedish population-based registers, the aims of the present study were 2-fold: (1) to examine whether a history of psoriasis influences reproductive patterns and (2) to investigate whether maternal psoriasis is associated with increased risk for adverse maternal and pregnancy outcomes.

METHODS

Data sources

We used information from Swedish population-based registers including the Multigeneration Register (MGR), Medical Birth Register (MBR), Patient Register, Cause of Death Register, and Total Population Register. Record linkages across registers were made possible by the 12-digit national registration number assigned to all Swedish residents at birth or time of first residency.

The Multigeneration Register. The MGR includes index persons born in 1932 or later who were alive in 1961 or later, with links to their parents, siblings, and children, including birthdates of all individuals.[9]

The Medical Birth Register. The MBR includes information on virtually all births in Sweden from 1973 onward.[10] Starting from the first antenatal visit, information is prospectively collected on demographic data; reproductive history; birth characteristics; and complications during pregnancy, birth, and the neonatal period. Information on smoking habits and prepregnancy body mass index (BMI) are available from 1983 and 1992, respectively. Since 1973, intrauterine stillbirths have been recorded from completed gestational week 28 or later, and, since 2008, from gestational week 22 or later. Complications during pregnancy and birth, including malformations, are classified according to the Swedish version of the International Classification of Diseases (ICD10 SE).[11] Based on a standardized form, the diagnoses are recorded at the time of discharge from the maternity ward.

The patient register. The Patient Register includes information on inpatient care, with each record containing date of admission and up to eight discharge diagnoses.[12] From 2001, outpatient visits to hospital clinics are included. Sweden used the seventh ICD revision (ie, ICD-7) until 1968, the ICD-8 between 1969 and 1986, the ICD-9 between 1987 and 1996, and the ICD-10 from 1997. From the Patient Register, we identified women hospitalized or treated on an outpatient basis for psoriasis. We also identified malformations in their children reported within 3 years of birth.

The cause of death register. Since 1952, the Cause of Death Register has recorded all deaths of Swedish residents, including date of death and main and contributing causes of death according to the ICD classification. The number of nonreported events is low, estimated at less than 1%.[13]

The population register. The Swedish Population Register monitors the vital status of all residents,[14] including dates of immigration or emigration.

Study design

We defined 2 separate study populations. First, to examine reproductive patterns in women with and without psoriasis, we defined a cross-sectional study population of women identified in the MGR who were 40 years or older in 2009, which was the last year of the study (study population 1). Women who had died or emigrated before 2009 were excluded. Study population 1 encompassed 1 667 583 women assumed to have completed their childbearing period (at 40 years of age).

Second, to assess the association between psoriasis and maternal and pregnancy outcomes, we defined a study population of births between 1992 and 2009 (study population 2), a period during

Abbreviations used:

BMI:	body mass index
CI:	confidence interval
ICD:	International Classification of Diseases
ICD10 SE:	Swedish version of the International Classification of Diseases, 10th revision
MGR:	Multigeneration Register
MBR:	Medical Birth Register
OR:	odds ratio

which information on maternal smoking status and prepregnancy BMI was available in the MBR. Only births with complete information for all variables in the model were included in the analysis. After the exclusion of 274 367 births with incomplete information on smoking status and/or BMI (15.8% of all births), study population 2 included 1 464 517 births in 672 658 unique women.

Defining psoriasis, reproductive history, and birth outcomes

Psoriasis was defined as having a record of primary or secondary diagnosis of psoriasis (ICD-7: 706.0; ICD-8: 696.00-696.19; ICD-9: 696A, 696B; ICD-10: L40) identified either in the inpatient records (1964-2009) or the outpatient records (2001-2009) of the Patient Register, irrespective of time point in relation to births. Reproductive history (age at first birth, time between births, final parity) for women in study population 1 was obtained from the MGR. Data on pregnancy characteristics, birth outcomes, prepregnancy BMI (defined as prepregnancy weight [in kilograms] divided by height × height [in meters]), and smoking at first antenatal visit (0, 1-9, 10+ cigarettes/d) were retrieved from the MBR. Information on congenital malformations in the MBR was supplemented with data on malformations recorded in the Patient Register within 3 years of birth (for ICD-codes, see Supplemental Table I; available via Mendeley at http://dx.doi.org/10.17632/3zhjv9hhfc.1).

Preterm birth was defined as a birth before gestational week 37. Neonatal mortality was defined as newborn's death within 27 days of birth. *Large* and *small for gestational age* were defined, respectively, as weight above or below the mean weight for gestational age ±2 standard deviations.[15]

Statistical methods

To compare reproductive patterns between women with and without psoriasis, we calculated proportions of parous/nulliparous women, distributions and mean differences in age at first and last births, intervals between childbirths, and total parity by psoriasis status. Means and proportions were assessed nonparametrically using the *t* test and the chi-squared test, respectively. Linear regression models were used to estimate mean differences while adjusting for age and parity. Additionally, standardized mean differences were calculated as measures of effect size.[16,17]

To investigate associations between psoriasis and maternal characteristics and between psoriasis and adverse pregnancy outcomes, we used logistic regression to estimate odds ratios (ORs) with 95% confidence intervals (CIs). Models were adjusted based on a priori knowledge of factors associated with both the risk of psoriasis and the outcomes under study. In a separate step, we examined whether the effect of maternal psoriasis on pregnancy outcomes differed by smoking history or maternal BMI. All models were adjusted for the intrasibling correlation among children by using a robust estimator of the standard errors with the mother as the cluster variable.[18] Only births with complete information on all covariates in the models were included in the analyses. Among births with complete covariate information, 1.09% were exposed to psoriasis, whereas among births with incomplete information, 1.14% were exposed to psoriasis, indicating no difference in exposure between those included and excluded in the analyses.

The study was approved by the Stockholm Ethics Review Board.

RESULTS

Reproductive patterns

Among 1 667 583 women aged 40 years or older in 2009 (study population 1), 33 488 (2%) had a diagnosis of psoriasis. Although the proportion of nulliparous women was slightly lower in women with psoriasis compared with women with no record of psoriatic disease (12.1% and 12.8%, respectively), mean parity at the end of the reproductive period did not differ. In parous women, age at first birth was younger (23.6 vs 24.6 years) in women with psoriasis. In women with 2 or more births, both the overall mean time interval between first and last pregnancy and mean interpregnancy intervals were longer in women with psoriasis (Table I).

Maternal characteristics

Table II shows the distribution of maternal characteristics by psoriasis status. Smoking, overweight, and obesity was more common in women with psoriasis.

Table I. Reproductive patterns (parity, age at first birth, pregnancy intervals) in 1 667 583 women with and without psoriasis, aged 41 to 77 years (born 1932-1968), alive and residents of Sweden in 2009 (study population 1)

Characteristics	Psoriasis N = 33 488	No psoriasis N = 1 634 095	*P* value[*,†]
Age			
Age in years in 2009, mean (SD)	59.7 (9.5)	57.7 (10.2)	<.001
Age in years in 2009 (birth year), n (%)			
41-49 (1960-1968)	6014 (18.0)	441 012 (27.0)	<.001
50-59 (1950-1959)	9333 (27.9)	456 720 (28.0)	
60-69 (1940-1949)	12 408 (37.1)	480 697 (29.4)	
70-77 (1932-1939)	5733 (17.1)	255 666 (15.7)	
Parity			
Total parity, n (%)			
0 children	4049 (12.1)	209 702 (12.8)	<.001
1 children	5314 (15.9)	234 992 (14.4)	
2 children	13 965 (41.7)	703 566 (43.1)	
3 children	7194 (21.5)	352 951 (21.6)	
4 children	2165 (6.5)	97 125 (5.9)	
5+ children	801 (2.4)	35 759 (2.2)	
Total parity, mean (SD)	2.03 (1.19)	2.01 (1.18)	.014
Mean difference[‡] (95% CI)	0.016 (0.003-0.029)	0.000 (ref)	
Mean difference[§] (95% CI)	0.013 (0.000-0.025)	0.000 (ref)	
Standardized mean difference	0.014		
Age at first birth			
Age in years at first birth,[‖] n (%)			
<20	6087 (20.7)	209 987 (14.7)	<.001
20-24	12 541 (42.6)	555 392 (39.0)	
25-29	7360 (25.0)	431 151 (30.3)	
30-34	2542 (8.6)	164 636 (11.6)	
35-39	761 (2.6)	52 965 (3.7)	
≥40	148 (0.5)	10 262 (0.7)	
Missing	4049	209 702	
Age at first birth,[‖] mean (SD)	23.6 (4.81)	24.6 (4.98)	<.001
Mean difference[‡] (95% CI)	−1.05 (−1.11 to −1.00)	0.00 (ref)	
Mean difference[¶] (95% CI)	−0.81 (−0.86 to −0.76)	0.00 (ref)	
Standardized mean difference	0.21		
Age at last birth			
Age at last birth,[‖] n (%)			
<20	851 (2.9)	27 736 (2.0)	<.001
20-24	5202 (17.7)	197 416 (13.9)	
25-29	10 447 (35.5)	480 128 (33.7)	
30-34	8329 (28.3)	448 055 (31.5)	
35-39	3745 (12.7)	220 038 (15.5)	
≥40	865 (2.9)	51 020 (3.6)	
Missing	4049	209 702	
Age at last birth,[‖] mean (SD)	29.0 (5.31)	29.8 (5.23)	<.001
Mean difference[‡] (95% CI)	−0.81 (−0.87 to −0.75)	0.00 (ref)	
Mean difference[¶] (95% CI)	−0.62 (−0.67 to −0.56)	0.00 (ref)	
Standardized mean difference	0.16		
Interval between first and last birth,[#] mean (SD) (reproductive period)	6.55 (4.57)	6.14 (4.34)	<.001
Interpregnancy interval			
Interpregnancy interval,[#,**] mean (SD)			
Overall, women with ≥2 children	4.18 (2.45)	3.96 (2.29)	<.001
Women with 2 children	4.21 (2.82)	3.95 (2.60)	<.001
Women with 3 children	4.26 (1.94)	4.08 (1.85)	<.001
Women with 4 children	3.94 (1.48)	3.83 (1.41)	.002

Continued

Table I. Cont'd

Characteristics	Psoriasis N = 33 488	No psoriasis N = 1 634 095	*P* value*,†
Women with 5+ children	3.45 (1.08)	3.36 (1.04)	.009
Overall mean difference‡ (95% CI)	0.22 (0.19; 0.25)	0.00 (ref)	
Overall mean difference¶ (95% CI)	0.16 (0.13; 0.19)	0.00 (ref)	
Standardized mean difference	0.10		

CI, Confidence interval; *ref*, reference; *SD*, standard deviation.
*From chi-squared test.
†From *t* test, assuming independent observations and equal variances.
‡From linear regression, unadjusted.
§From linear regression, adjusted for age in 2009 (woman's birth year).
‖Among women with ≥1 child.
¶From linear regression, adjusted for age in 2009 (woman's birth year) and parity.
#Among women with ≥2 children.
***Interpregnancy interval* (IPI) defined as the interval between the births of consecutive children. Women with 3 children contribute 2 IPIs, women with 4 children contribute 3 IPIs, and so on.

Maternal and pregnancy adverse outcomes

Among 1 464 517 births between 1992 and 2009 (study population 2), 15 975 (1.1%) were exposed to maternal psoriasis. In adjusted multivariable analyses, maternal psoriasis was associated with elevated risk of pregnancy hypertension (OR, 1.37; 95% CI, 1.19-1.58), premature rupture of membranes (OR, 1.15; 95% CI, 1.04-1.27), and large for gestational age (OR, 1.11; 95% CI, 1.01-1.21) (Table III available via Mendeley at http://dx.doi.org/10.17632/3zhjv9hhfc.1).

ORs for preterm birth, stillbirth, and neonatal mortality were elevated but were not statistically significant after adjustments. There was no evidence of effect modification by maternal BMI, with the exception of pregnancy hypertension, for which the effect was most pronounced in obese women (OR, 1.54; 95% CI 1.21-1.97).

Malformations

After adjustments, there was an association between maternal psoriasis and cleft palate (OR, 1.69; 95% CI, 1.07-2.66) and unspecified malformations (OR, 1.08; 95% CI, 1.01-1.16) in the children (Table IV available via Mendeley at http://dx.doi.org/10.17632/3zhjv9hhfc.1). These associations were based on 19 and 862 cases, respectively, exposed to maternal psoriasis.

DISCUSSION

Based on information available in Swedish population-based registers, we aimed to improve the understanding of reproductive patterns and maternal and pregnancy outcomes in women with psoriasis.

Reproductive patterns

We found no evidence that fertility is negatively affected in women with psoriasis. There was no difference in mean parity at the end of the reproductive period between women with and without psoriasis. If anything, nulliparity was less common in women with psoriasis. Also, on average, women with psoriasis were younger at first birth, and the mean time between first and last birth and the mean interpregnancy interval were longer. Our findings may reflect informed choices on the part of women with psoriasis when planning a family because some systematic treatments are contradicted during pregnancy because of risk of adverse events, including possible negative effects on future fertility.[3] Also, many women experience symptom relief during pregnancy.

Maternal and pregnancy outcomes

Women with psoriasis were at increased risk for pregnancy hypertension and premature rupture of membranes. Although we found no evidence of increased risk of preterm birth, still birth, or neonatal mortality, women with psoriasis were at an increased risk of giving birth to large-for-gestational-age newborns.

Malformations

In an analysis based on data on malformations from 2 independent register sources and adjusted for maternal smoking and prepregnancy BMI, we found statistically significant associations between exposure to maternal psoriasis and cleft palate and unspecified malformations in the children. Despite the large data set at hand, the findings related to cleft lip were based on few events and should be interpreted with caution.

When assessing pregnancy risks in chronic conditions with an inflammatory component, it is challenging to distinguish systemic effects of the

Table II. Distribution and association between maternal and childbirth characteristics based on 1 464 517 births exposed and unexposed to maternal psoriasis (study population 2)

	Births exposed to psoriasis (N = 15 975)	Births unexposed to psoriasis (N = 1 448 542)	Risk of psoriasis	
Outcome	**n (%)***	**n (%)***	**OR† (95% CI)**	**OR‡ (95% CI)**
Maternal age at childbirth in years				
<20	318 (2.0)	26 872 (1.9)	1.00	1.00
20-29	7834 (49.0)	706 513 (48.8)	0.94 (0.84 to 1.05)	1.06 (0.95 to 1.19)
30-39	7323 (45.8)	676 335 (46.7)	0.91 (0.81 to 1.03)	1.09 (0.97 to 1.23)
40-54	500 (3.1)	38 822 (2.7)	1.09 (0.94 to 1.26)	1.24 (1.07 to 1.44)
Calendar period				
1992-1997	5898 (36.9)	486 804 (33.6)	1.00	1.00
1998-2003	5169 (32.4)	432 461 (29.9)	0.99 (0.95 to 1.03)	1.02 (0.98 to 1.06)
2004-2009	4908 (30.7)	529 277 (36.5)	0.77 (0.73 to 0.80)	0.81 (0.78 to 0.85)
Maternal smoking, cigarettes/d				
0	12 225 (76.5)	1 271 660 (87.8)	1.00	1.00
1-9	2438 (15.3)	120 477 (8.3)	2.10 (2.00 to 2.22)	2.02 (1.92 to 2.14)
10+	1312 (8.2)	56 405 (3.9)	2.42 (2.26 to 2.59)	2.25 (2.10 to 2.41)
Maternal body mass index, kg/m^2				
<25	9246 (57.9)	967 593 (66.8)	1.00	1.00
25-29	4338 (27.2)	341 988 (23.6)	1.33 (1.27 to 1.39)	1.32 (1.26 to 1.37)
≥30	2391 (15.0)	138 961 (9.6)	1.80 (1.70 to 1.91)	1.75 (1.65 to 1.86)

CI, Confidence interval; *n*, number of childbirths; *OR*, odds ratio.
*Due to rounding, not all percentages add up to 100.
†Estimated from univariable logistic regression.
‡Estimated from multivariable logistic regression including all tabulated covariates.

disease from the possible influence of treatment, lifestyle, and comorbidities. In a study that examined the prevalence of modifiable risk factors for adverse pregnancy outcomes, women with psoriasis were more likely to be overweight or obese, smoke, and have a diagnosis of depression compared with control individuals.[19] Similarly, a Danish study found that smoking and obesity were more common in women with psoriasis.[20] Also, a recent Danish-Swedish study reported that diabetes, hypertension, and depression were more common in women with psoriasis, as assessed by patterns of drug use.[8] In the present study, the prevalence of both smoking and high BMI were higher in women with psoriasis. Although our results were adjusted for BMI and smoking, it cannot be ruled out that the observed increased risk for adverse pregnancy outcomes in women with psoriasis reflect an influence from comorbidities, lifestyle, or treatment.

Most studies to date on adverse pregnancy outcomes in women with psoriasis have been hampered by small size, which may in part explain divergent findings. An Australian study encompassing 145 births in women with psoriasis and 860 births to women without psoriasis found an increased risk of recurrent abortions, hypertension, and caesarean birth in women with psoriasis.[21]

In contrast to our findings, a Taiwanese record-linkage study that included 1463 mothers with psoriasis and 11 704 control mothers found that women with severe psoriasis were at an increased risk of giving birth to low-birth-weight infants. No excess risk was observed in women with mild psoriasis.[22]

In a cohort study based on information from medical records in 1 Israeli center, women with psoriasis were at an increased risk of spontaneous or induced abortions, pregnancy hypertension, premature rupture of membranes and large for gestational age.[23]

A 2-fold increased risk of poor outcome composite, including preterm birth and low birth weight, was found in a retrospective cohort study in the United States. In the same study, psoriasis was not associated with the risk of caesarean birth and spontaneous abortion. Small numbers precluded assessment of the risk of pre-eclampsia.[24]

A study based on self-reported data encompassing 87 000 pregnancies in the national Danish Birth Cohort between 1996 and 2007 found no increased risk of fetal deaths in women with mild to moderate psoriasis.[20] Also, similar to our findings, fertility in women with psoriasis appeared to be unaffected because no prolonged time to pregnancy could be detected.

Differences in study design, data materials, analytical approach, and periods covered may explain differences in findings between our study and a recently published study based on information combined from registers in Denmark and Sweden including 8097 singleton births in 6103 women with psoriasis and 964 births in 753 women with psoriatic arthritis between 2007 and 2012.[8] Treatment data from prescription registers were used as a surrogate for comorbidities and severity of psoriasis. Similar to our findings, an increased risk of pregnancy hypertension was observed. In addition, the Danish-Swedish study found elevated risk for pregnancy diabetes, pre-eclampsia, and elective and emergency cesarean birth in women with psoriasis, with the highest risk observed in women with severe psoriasis, who also were at increased risk of preterm birth and low birth weight.

Including more than 15 000 births to women with psoriasis, the present study, to our knowledge, is the largest to date addressing maternal and pregnancy outcomes. Additional strengths include the population-based design, covering women with a record of a psoriasis diagnosis in the nationwide Patient Register. Information on malformations was obtained from 2 independent sources, the MBR and the Patient Register. Similar to most previous studies in this area, individual-level data on type and duration of treatment were unavailable. Limitations also included the absence of information on lifestyle factors, comorbidities, and other potential confounders. However, by using data from the Medical Birth Register, we were able to adjust for prepregnancy BMI and smoking status recorded in the first trimester. Also, the data set at hand did not include information on severity of disease, but based on information in the Patient Register, most of the included women with psoriasis were likely to have had moderate or severe disease. Thus, because our study did not include cases managed solely in primary care, results cannot immediately be generalized to all women with psoriasis.

Given the generally early age of onset of psoriasis, we chose to also include women with a first recorded diagnosis of psoriasis after childbirth to avoid differential misclassification. It can be assumed that the majority of women—including among those with a diagnosis after childbirth—had signs and symptoms of psoriasis before specialist health care contact, with children likely to have been exposed to any systemic effect of psoriasis.

Despite the large study population, small numbers and the absence of treatment data hampered the interpretation of findings on rare outcomes, particularly with regard to malformations. Although we found an association between maternal psoriasis and cleft palate, any such risk increase would translate into very few additional cases because of very low incidence rates.

CONCLUSION

The results of this large population-based register study provide no evidence that fertility is negatively affected in women with psoriasis. Although we found no increased risk for preterm birth, stillbirth, or neonatal mortality, women with psoriasis were at increased risk for pregnancy hypertension, premature rupture of membranes, and giving birth to large-for-gestational-age infants. Based on few events, we found an association between maternal psoriasis and cleft palate in the children. Given the conflicting results reported across studies, there is a need for future studies based on detailed individual-level information to address the role of adverse outcomes associated with disease characteristics, comorbidities, treatment, and lifestyle factors.

REFERENCES

1. Parisi R, Symmons DP, Griffiths CE, et al. Global epidemiology of psoriasis: a systematic review of incidence and prevalence. *J Invest Dermatol*. 2013;133(2):377-385.
2. Horn EJ, Chambers CD, Menter A, Kimball AB, International Psoriasis C. Pregnancy outcomes in psoriasis: why do we know so little? *J Am Acad Dermatol*. 2009;61(2):e5-e8.
3. Rademaker M, Agnew K, Andrews M, et al. Psoriasis in those planning a family, pregnant or breast-feeding. The Australasian Psoriasis Collaboration. *Australas J Dermatol*. 2018;59(2):86-100.
4. Mecacci F, Pieralli A, Bianchi B, Paidas MJ. The impact of autoimmune disorders and adverse pregnancy outcome. *Semin Perinatol*. 2007;31(4):223-226.
5. Baird DD, Narendranathan M, Sandler RS. Increased risk of preterm birth for women with inflammatory bowel disease. *Gastroenterology*. 1990;99(4):987-994.
6. Cornish J, Tan E, Teare J, et al. A meta-analysis on the influence of inflammatory bowel disease on pregnancy. *Gut*. 2007;56(6):830-837.
7. Bobotsis R, Gulliver WP, Monaghan K, Lynde C, Fleming P. Psoriasis and adverse pregnancy outcomes: a systematic review of observational studies. *Br J Dermatol*. 2016;175(3):464-472.
8. Bröms G, Haerskjold A, Granath F, Kieler H, Pedersen L, Berglind IA. Effect of Maternal Psoriasis on Pregnancy and Birth Outcomes: A Population-based Cohort Study from Denmark and Sweden. *Acta Derm Venereol*. 2018;98(8):728-734.
9. The Multi-Generation Register. Available at: http://www.scb.se/en_/Finding-statistics/Publishing-calendar/Show-detailed-information/?publobjid=1874. Accessed July 3, 2019.
10. The Swedish Medical Birth Register. Available at: http://www.socialstyrelsen.se/register/halsodataregister/medicinskafodelseregistret/. Accessed July 7, 2019.
11. Sjukdomsklassifikation ICD-10. Available at: https://www.socialstyrelsen.se/utveckla-verksamhet/gemensam-informationsstruktur/klassificering-och-koder/icd-10/. Accessed July 3, 2019.

12. The National Patient Register. Available at: https://www.socialstyrelsen.se/en/statistics-and-data/registers/alla-register/the-national-patient-register/. Accessed July 3, 2019.
13. The Cause of Death Register. Available at: https://www.socialstyrelsen.se/statistik-och-data/register/alla-register/dodsorsaksregistret. Accessed July 3, 2019.
14. The National Population Register. Available at: https://www.scb.se/vara-tjanster/bestalla-mikrodata/vilka-mikrodata-finns/individregister/registret-over-totalbefolkningen-rtb. Accessed July 3, 2019.
15. Marsal K, Persson PH, Larsen T, Lilja H, Selbing A, Sultan B. Intrauterine growth curves based on ultrasonically estimated foetal weights. *Acta Paediatr*. 1996;85(7):843-848.
16. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. 2nd ed. Hillsdale, NJ: Erlbaum; 1988.
17. Faraone SV. Interpreting estimates of treatment effects: implications for managed care. *P T*. 2008;33(12):700-711.
18. Rogers WH. Regression standard errors in clustered samples. *STATA Tech Bull*. 1994;13:19-23.
19. Bandoli G, Johnson DL, Jones KL, et al. Potentially modifiable risk factors for adverse pregnancy outcomes in women with psoriasis. *Br J Dermatol*. 2010;163(2):334-339.
20. Harder E, Andersen AN, Kamper-Jorgensen M, Skov L. No increased risk of fetal death or prolonged time to pregnancy in women with psoriasis. *J Invest Dermatol*. 2014;134(6):1747-1749.
21. Ben-David G, Sheiner E, Hallak M, Levy A. Pregnancy outcome in women with psoriasis. *J Reprod Med*. 2008;53(3):183-187.
22. Yang YW, Chen CS, Chen YH, Lin HC. Psoriasis and pregnancy outcomes: a nationwide population-based study. *J Am Acad Dermatol*. 2011;64(1):71-77.
23. Cohen-Barak E, Nachum Z, Rozenman D, Ziv M. Pregnancy outcomes in women with moderate-to-severe psoriasis. *J Eur Acad Dermatol Venereol*. 2011;25(9):1041-1047.
24. Lima XT, Janakiraman V, Hughes MD, Kimball AB. The impact of psoriasis on pregnancy outcomes. *J Invest Dermatol*. 2012;132(1):85-91.