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A Population-based Study of Perinatal Infection Risk in Women With and Without Systemic Lupus Erythematosus and Their Infants

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Abstract

Background—Increased risk of adverse birth outcomes is well described in women with systemic lupus erythematosus (SLE), but risk of maternal or infant infection in the peripartum period has not been well studied. We conducted a population-based cohort study of infection risk in women with and without SLE and their infants.

Methods—Linked birth-hospital discharge data identified 1,297 deliveries to women with SLE and a 4:1 comparison cohort of deliveries to women without SLE in Washington State, 1987–2013. Maternal and infant infections during the first 30 days after delivery were identified. Relative risks (RR) and 95% confidence intervals (CI) were estimated.

Results—Women with SLE were 1.7 times more likely (95% CI 1.4, 2.0) to have an infection during the birth hospitalization and more likely to receive antibiotics during labor (RR 1.3, 95% CI 1.1, 1.5), though there was no increased risk of chorioamnionitis in women with SLE. Infants of women with SLE had an increased risk for an infection during the birth hospitalization (RR 2.2, 95% CI 1.3, 3.5), although the size of the difference was smaller when adjusted for gestational age (RR 1.4, 95% CI 0.9, 2.1). Risks of neonatal infection, sepsis, receipt of antibiotics, and admission to neonatal intensive care were also increased, and were also attenuated after adjustment for gestational age.

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Conclusions—Women with SLE have an increased risk of peripartum infections and antibiotic exposure. Their neonates have a greater likelihood of infection, much of which is attributable to preterm birth.

Introduction

Many women with systemic lupus erythematosus (SLE) have compromised immunity, due to both the disease process and the immunosuppressive medications often prescribed for management¹. Persons with SLE are known to have a greater risk of infection, which may account for up to 25% of all deaths in this population^{2,3}. Although many studies have described relatively poor pregnancy outcomes in women with SLE and their infants, few studies have specifically addressed the infection risk in the mother during the perinatal period^{4,5}. Infection in women with SLE can also potentially be an important consideration for their offspring, as the baby is susceptible to infections via vertical transmission of maternal infection *in utero* or at the time of delivery. Additionally, neonates have immature immune systems and partially rely on borrowed immunity from their mother in the form of transplacentally-transmitted immunoglobulins (IgG), and IgA from breast milk in the first months of life⁶. The infant immune system is deficient early in life due to several mechanisms, including a decreased ability to produce inflammatory cytokines such as TNF- α and IL6, reduced neutrophil and dendritic cell function, decreased activation of natural killer cells, and minimal production of circulating immunoglobulins¹. Women with altered immunity due to SLE and immunomodulatory medications may be less capable of providing protective antibodies to their offspring⁷. Both maternal and infant peripartum infections are strongly associated with preterm birth.^{8,9} SLE has strong associations with both preterm birth and small-for-gestational age babies¹⁰. To our knowledge, no studies have addressed infection risk to infants of mothers with SLE. Such studies could provide important information to healthcare providers for women with SLE for the purpose of both counseling and monitoring during pregnancy and following delivery. We therefore designed a population-based cohort study to evaluate the risk of perinatal infection and antibiotic use in women with SLE compared to women without SLE, and to evaluate infection-related risk in their offspring during the neonatal period.

Methods

This population-based cohort study used linked birth-hospital discharge records from Washington State from 1987–2013. Birth records were linked to hospital discharge records from the Comprehensive Hospital Abstract Reporting System (CHARS), the state-wide hospital discharge database that includes all hospitalizations at non-government facilities in Washington State. As only de-identified data were accessed, this study was determined to be exempt from Human Subjects Protection Committee review by the Washington State Institutional Review Board.

Women were considered to have SLE if the International Classification of Diseases, 9th Revision (ICD-9) code 710.0 “Systemic Lupus Erythematosus” was present in the hospital discharge record for the delivery hospitalization. We identified 1,297 women identified with SLE who had singleton deliveries during the study years. For comparison, 5,584 women

without SLE were selected randomly from the remaining singleton deliveries, frequency-matched (~4:1) on year of delivery to women with SLE. In our evaluation of maternal characteristics and outcomes, we included all data pertaining to the delivery hospitalization, which included pregnancies that resulted in fetal deaths (23 women with SLE; 31 comparators). To examine neonatal outcomes, only live births were included.

We evaluated the following maternal infection outcomes: chorioamnionitis, receipt of antibiotics during labour, or a diagnosis of any infection during the maternal delivery hospitalization. Chorioamnionitis was defined if a relevant ICD9 code (762.7 or 658.4) was indicated in the hospital discharge record, or if the check box on the birth record indicated “Clinical chorioamnionitis or maternal temperature >38.0C° during labor.” Maternal receipt of antibiotics was similarly ascertained in the birth record for deliveries 2003 or later. Maternal infections included all relevant ICD9 codes for any infection (online Supplementary Material) with the exception of dermatophytoses and HPV, which were not included because these non-invasive infections were unlikely to be either SLE-related or important as peripartum infections, and asymptomatic bacteriuria and Group B Strep colonization, which we considered infection risk-factors rather than indicators of current infection; all other possible infections including bacterial, viral, parasitic, and fungal infection listings in the ICD9 were included. We identified women with renal involvement during the delivery hospitalization by presence of ICD9 580.0–587.9, which includes the categories of nephritis, nephropathy, and acute and chronic renal failure (both SLE-specific and non-specific); no comparison women had any of these codes recorded.

We restricted offspring outcomes to the neonatal period, defined as the first 30 days of life. As we were interested in whether compromised maternal immunity leads to increased infection risk in the baby, such risk would be greatest in the neonatal period when the baby is most reliant on the mother’s transplacentally-derived immunoglobulins for protection. Additionally, because we could only measure infections resulting in hospitalization subsequent to the birth hospitalization, ascertainment of these in our study would be nearly complete only during the neonatal period, when infants are almost uniformly hospitalized for fever or suspicion of infection. We evaluated the following outcomes in neonates: infection during the birth hospitalization, receipt of anti-sepsis antibiotics during the birth hospitalization, infection indicated in any subsequent hospitalization within the neonatal period, any infection within 30 days of life (“neonatal infection”), and neonatal sepsis. Neonatal infection was a composite outcome of infection during the birth hospitalization and any infection-associated readmissions within 30 days of birth. Neonatal sepsis included a subset of the neonatal infection outcome, limited to ICD9 codes including the terms “sepsis,” “septicemia,” or “bacteremia.” Admission to the Neonatal Intensive Care Unit (NICU) was also evaluated. Infant infections during the birth hospitalization and re-hospitalization were determined by screening hospital discharge records using the same ICD9 criteria as maternal infection except where defined differently based by age (Supplementary Table A). Receipt of antibiotics and admission to the NICU were identified in birth records for deliveries in 2003 or later.

A stratified analysis for the risk of these infection-related outcomes was performed to compare outcomes among women with and without SLE using Mantel-Haenszel relative-

risk (RR) estimates and 95% confidence intervals (CI). Based on known or suspected determinants of adverse pregnancy and infant outcomes,^{11,12} after a prior adjustment for maternal age (<20, 20–34, 35+ years), we evaluated the following co-variables as potential confounders: delivery year (before or after 2005), prenatal smoking, maternal education (< high school, high school, college, or graduate education), gestational age at delivery (<37, 37+ weeks), number of prior live births (0,1,2+), race/ethnicity (white, black, Asian/Pacific Islander, Hispanic and other), cesarean-section delivery (yes/no), diabetes (yes/no including prevalent and gestational), and whether the infant was being breast fed at discharge from the birth hospitalization. We limited the number of gestational age categories due to the low prevalence of preterm delivery in the non-SLE group and even lower prevalence of post-term deliveries in both groups. Race/ethnicity was defined per mother self-identification on birth records wherein only one primary designation was provided. Unless otherwise indicated, all outcomes were adjusted for maternal age only, as none of the other factors indicated above meaningfully altered the risk estimates (by >10%).

These variables were also assessed as possible effect modifiers, with the exception that birthweight was evaluated as a potential effect modifier for infant outcomes, but not evaluated as a possible confounder due to the high degree of collinearity with gestational age (87% agreement between birthweight category and gestational age in our cohort). Effect modification was evaluated by Chi square tests of homogeneity and the presence of important differences in stratum-specific RRs. For maternal outcomes, the effect of body mass index (BMI) was evaluated in subgroup analyses, as these data were only available after 2002. We stratified analyses for the outcome of NICU admission by maternal prenatal smoking status due to a suggestion of effect modification in the data. We used linear regression with an interaction of SLE and smoking to evaluate the effect of smoking on gestational length for women with and without SLE. We present infant outcomes adjusted for maternal age, and then additionally adjusted for preterm delivery in order to better demonstrate the direct effects of SLE on infection, considering that preterm delivery is part of one causal pathway to infection¹³, but is presumed to be an incomplete and non-requisite mediator; we also therefore present results stratified by preterm birth.

We additionally performed mediation analysis for the effect of gestational age on the association between maternal SLE and the outcomes of birth-hospitalization infection and NICU admission, using the *medeff* and *medsens* functions of Moremata package in STATA¹⁴, again with adjustment for maternal age and smoking. This mediation analysis uses 1000 simulations to estimate the incidence of the outcome under each specified condition, including under absence of the mediating condition. This method outputs the *Average Causal Mediated Effect* (ACME) and the *Total Effect*, the proportion of which (ACME/Total Effect) gives “percent mediation”, which in this scenario provides a quantitative estimate of how the disproportionate rate of preterm birth in women with SLE influences the risk of infection or NICU admission^{15,16}. We used E-value to estimate the minimum unmeasured confounding in the age-adjusted risk estimates for these outcomes that would be required to explain the observed effect size¹⁷.

Maternal and infant length of stay (LOS; categorized as <3 vs. 3+ days) during the delivery hospitalization were not included as covariates in our analyses because longer LOS could

also be a consequence of infection. We performed a separate analysis of the relationship between maternal SLE and LOS in both mothers and infants, stratified by reported presence or absence of infection during that hospitalization.

RESULTS

Women with SLE were older than women without this illness, and had more prior pregnancies, were less likely to be white, unmarried, or to smoke, were more highly educated, more often had cesarean-section delivery, and had a longer hospital stay at delivery (Table 1). Nephritis, nephropathy, or renal failure was noted in delivery hospitalization records of 7% of women with SLE (vs. none in comparison women). Infants of women with SLE were slightly less likely to have been breast fed prior to discharge and were more likely to be preterm, low birthweight, and have a longer birth hospitalization compared to infants of women without SLE.

A greater proportion of women with (14%), than without SLE (8%) had an infection noted during the birth hospitalization, RR 1.7 (95% CI 1.4, 2.0, Table 2). 30% of women with, compared to 23% of women without SLE received antibiotics during labor RR 1.3 (95% CI 1.1, 1.5). In a subgroup analysis of deliveries between 2003 –2013 (years with BMI data available), among underweight and normal weight women, those with SLE were 1.4 times (95% CI, 1.2, 1.7) more likely to receive antibiotics during labor compared to women without SLE; the association was not present for overweight women. The associations of SLE with infection and receipt of antibiotics were more marked in women with vaginal deliveries (RR 1.8, 95% CI 1.5, 2.3), and RR 1.4 (95% CI 1.2, 1.6), respectively). No increased risk of chorioamnionitis was observed for women with SLE during the birth hospitalization (Table 2). Women with SLE complicated by renal disease were more likely to have had an infection compared to women without SLE (RR 3.3, 95% CI 2.3, 4.7; data not shown). Risks were not different when stratified as before or after 2005, a date chosen for when hydroxychloroquine became more commonly used for SLE in pregnancy.

The RR for any infant infection during the birth hospitalization was 2.6 (95% CI 1.8, 3.8) for babies born to women with SLE (Table 3). After adjustment for gestational age, the RR was attenuated to 1.4 (95% CI 0.9, 2.1). Among term infants only, the RR was also 1.4 (95% CI 0.7, 2.7). Infants of women with SLE complicated by renal involvement had a greater risk of infection, RR 5.8 (95% CI 2.6, 3.1), which was markedly attenuated with adjustment for gestational age, RR 1.6 (95% CI 0.7, 3.7; data not shown). Similarly, in babies of women with SLE, the RR for receiving anti-sepsis antibiotics during the birth hospitalization was 2.2 (95% CI 1.3, 3.5), but after adjustment for gestational age the risk was diminished (Table 3). No increased risk of infection-related re-hospitalization within 30 days was observed, whether adjusted or unadjusted for gestational age. The risk of any infection within 30 days from birth (any neonatal infection) was 1.8 times greater in babies born to of women with SLE (95% CI 1.3, 2.6), but there was little evidence of excess risk if adjusted for gestational age. Similarly, neonatal sepsis was more frequent in babies born to women with SLE, RR 2.3 (95% CI 1.4, 3.6), but this association decreased after adjustment for gestational age. No other covariates, including maternal diabetes or breastfeeding modified the risk of neonatal infections. In mediation analyses evaluating the effect of preterm birth on infection

occurrence (adjusted for maternal smoking and age), 59% (95%CI 43,100) of the risk of birth hospitalization infections associated with SLE could be attributed to preterm birth (ACME/Total Effect). This analysis was sensitive to confounding however, with a small correlation between any confounder on preterm delivery and infection nullifying any mediating effect (ACME= 0 if $p > 0.20$, Supplementary Figure). The E-value was 2.1 for an unmeasured confounder associated with both preterm birth and infant infection that could explain away the gestational-age adjusted RR (E-value for CI; 1.0).

The RR of NICU admission in relation to maternal SLE status differed for infants of women who did, RR 6.6 (95% CI 3.6, 12.0) and did not smoke prenatally, RR 2.6 (95% CI 2.0, 3.3); adjustment for gestational length reduced, but did not completely attenuate the magnitude of these results. Mediation analysis attributed 31% of the excess risk of NICU admission in offspring of smokers with SLE (95%CI 23, 50; ACME=0 if $p > 0.30$, Supplementary Figures), and 64% of the risk in offspring of non-smokers with SLE to preterm birth (95%CI 44,100; ACME=0 if $p > 0.30$). The E-value for an unmeasured confounder associated with both preterm birth and NICU admission that could explain the observed gestational-age adjusted RR for NICU admission was 6.1 (for CI, 3.0) in maternal smokers and 1.9 (for CI, 1.0). In subgroup analysis of deliveries between 2003 and 2013, adjustment for maternal diabetes did not affect these associations. We confirmed the presumed effect modification of maternal smoking on the gestational length ($p=0.001$ for interaction), which did not account for the entirety of the differential risk of NICU admission between offspring of smokers and non-smokers with SLE (data not shown).

In an attempt to clarify whether babies born to mothers with SLE were more likely to require additional observation for sepsis and/or treatment of other conditions after birth, we evaluated length of birth hospitalization for offspring. Nosocomial infections may have also resulted from longer hospitalization, as well as further delaying discharge. Infants without infections born to women with SLE had prolonged birth hospitalizations compared to those without maternal SLE, RR 1.4 (95% CI 1.3, 1.6) However, infants who were diagnosed with infection had longer hospitalizations regardless of if the mother had SLE, adjusted for gestational age: RR 2.0 (95% CI 1.9, 2.2), though there was no difference for infants of mothers with or without SLE if the infant had been diagnosed with an infection. LOS was also longer for women with SLE compared to women without SLE, regardless of whether delivery was vaginal or by cesarean section, or whether or not complicated by infection (Supplementary Table B).

Comment

Main finding

These results suggest that women with SLE have a greater infection risk in the perinatal period compared to women without SLE. Women with SLE and renal disease were at even greater risk of infections. Infants of affected mothers had a greater risk of infection and of admission to the NICU during the birth hospitalization, and a greater risk of sepsis or any infection in the neonatal period. Notably, about half of this additional risk appeared to be mediated by the excess frequency of preterm birth, although increased risk of these outcomes remained present when considering only term pregnancies.

Interpretation

These findings are consistent with results of the few prior studies that have investigated this topic. Bauer et al studied 4,158 women whose delivery hospitalization was affected by severe sepsis and found SLE to be an independent risk factor for sepsis, adjusted OR 9.4 (95% CI 5.2, 16.7)⁴. Similarly, Clowse et al found that the incidence of sepsis during the delivery hospitalization was 0.5% in women with SLE compared with 0.1% in women without SLE, OR 3.5 (95% CI 2.0, 6.0), and the incidence of pneumonia was 1.7% in women with SLE vs. 0.2% in those without SLE, OR 4.3 (95% CI 3.1, 5.9).⁵ Plausible mechanisms for increased infection risk in women with SLE include treatment with immunosuppressive therapies as well as immune dysregulation from the disease process itself¹. In a systematic review and meta-analysis of pregnancy outcomes in women with SLE, the frequency of preterm birth in women with SLE was 39.4%¹⁹, whereas it was 23% in our population-based study, which likely included women with a broader spectrum of disease severity and activity than those included in SLE cohort studies. Inclusion of women in our study with lower activity or severity of disease may also explain why our risk estimates for infection were lower than those previously described. Passage of IgG from the mother to the baby increases dramatically with advancing gestational age, which partly explains why pre-term infants have greater infection risk⁶. A recent study utilizing Swedish birth registries reported that 21% of singleton births to women with SLE were complicated by infant infections, although this study did not address the interaction of preterm birth and infection¹⁸. In our study, preterm birth was likely a major, but not the sole mechanism leading to infection in neonates of women with SLE. Risk estimates for infection during the birth hospitalization, infection or sepsis in the neonatal period, and receipt of anti-sepsis antibiotics remained increased, but were considerably attenuated, after accounting for preterm delivery. Due to the broad indications for NICU admission, NICU admission is not a perfect surrogate for infection risk. However, understanding the risk of NICU admission independent of infection risk may be helpful for counseling women with SLE in the perinatal period.

Strengths of the study

This is one of the largest population studies to evaluate the risks of SLE in pregnant women on infectious complications to them and their infants. Although preterm birth is both a known risk factor for neonatal infection and a known complication of SLE in pregnancy^{20–23}, the risk of infection in infants born to women with SLE is still being further elucidated. We also evaluated the association between maternal SLE on infections, adjusted for gestational length, and then limited to only term infants, in order to evaluate the direct and indirect effects of SLE on risk of infection; these different risk estimates may be useful for counseling patients. Additional study strengths include full ascertainment of births and hospitalizations in this state during the study period. Our data on renal involvement in SLE, is to our knowledge, the first population-based evaluation including SLE and renal involvement.

Limitations of the data

This study had several limitations. Our reliance on ICD9 codes to identify SLE may have led to misclassification. The use of a single hospital discharge ICD9 code to identify persons with SLE has previously estimated an accuracy of 88%, with positive predictive value (PPV) of 99% and negative predictive value (NPV) of 87%.²⁴ However other reviews have placed the PPV estimate as low as 54–60% when based on a single hospitalization episode (sensitivity 98%, specificity 78%)²⁵. Misclassification of SLE due to use of a single ICD9 code in our study may have therefore resulted in bias towards toward the null. Although we were unable to assess the accuracy of ICD9 coding in the present study, we identified 62 women with ICD9 codes for SLE at delivery at one Washington state facility and reviewed their medical records; all of them had verification of this condition in their medical record. Although this was only conducted at a single hospital during recent years, it suggests that identification of SLE in this population at the time of delivery may be relatively accurate. We have no information about the accuracy of nephropathy as identified by ICD9 codes, although suspect it may be less sensitive for the presence of lower activity disease. We were also unable to assess SLE disease characteristics such as severity, presence of other, non-renal organ involvement, or immunomodulatory treatment regimen, precluding the possibility of identifying clinical features that might correlate most strongly with infection risk. Reliance on both ICD9 codes and birth certificate data for assessment of our outcomes could also have led to misclassification, though likely in a manner unbiased to the presence of maternal SLE. Although women may have had >1 delivery in our data during the study period, restriction of main analyses to first deliveries only did not alter results. Lastly, due to the rarity of outcomes such as chorioamnionitis, this study was underpowered to detect small increases in risk of these outcomes.

Conclusions

In summary, women with SLE, especially those with renal involvement, were observed to have an increased risk of peripartum infections and antibiotic use compared to women without SLE. Their infants had a greater infection risk during the neonatal period and a higher risk of admission to the NICU, with roughly half of the observed increased risk possibly attributable to preterm birth. Other factors associated with both preterm delivery and adverse infant outcomes in SLE, however, could be responsible for the observed mediation effect of preterm birth, given how sensitive these results were to unmeasured confounding. Providers caring for women with SLE should be aware of these risks as they treat patients during pregnancy and care for their infants. Future studies utilizing larger cohorts with detailed information about disease severity, specific immunomodulatory regimens, and infection outcomes would be useful to further characterize these risks of infection in the perinatal period.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1

Characteristics of women with and without systemic lupus erythematosus (SLE) with deliveries in Washington state, 1987 – 2013, and their singleton infants

<i>Maternal Characteristic at delivery</i>	Women with SLE (N=1,297)		Women without SLE (N=5,584)	
	N	% [*]	N	% [*]
Age (years)				
<20	34	2.6	503	9.0
20–29	588	45.3	2,894	51.8
30–34	418	32.2	1,389	24.9
35–39	209	16.1	651	11.7
40+	48	3.7	147	2.6
Race				
White	890	68.6	4,009	73.5
Black	74	5.7	221	4.1
Asian/Pacific Islander	156	12.0	482	8.8
Hispanic	94	7.2	606	11.1
Native American	53	4.1	13	2.5
Body Mass Index^a				
<18.5	26	4.0	98	3.5
18.5–24.9	312	47.8	1,284	46.2
25–29.9	151	23.1	741	26.7
≥30	164	25.1	657	23.6
Diabetes				
No	1,164	89.7	2,809	93.5
Yes	70	5.7	194	6.5
Nephritis, nephropathy, or renal failure complicating delivery	88	6.8	0	0
Education Level				
Less Than High School	102	7.9	901	18.5
Graduated High School	262	20.2	1,316	27.0
College	635	49.0	2,197	45.0
Graduate School	152	11.7	470	9.6
Marital Status				
Unmarried	338	26.1	1,705	30.6
Married	957	73.8	3,866	69.4
Smoking During Pregnancy				
No	1,125	86.7	4,760	87.3
Yes	135	10.4	695	12.7
Group B Strep culture positive^a				
No	584	80.8	2,453	81.7
Yes	126	17.4	550	18.3

C-Section				
No	813	62.7	4,263	76.4
Yes	484	37.3	1,319	23.6
Number of prior births				
0	539	41.6	2,278	41.5
1	406	31.3	1,763	32.1
2+	326	27.9	1,447	26.4
<hr/>				
Infant characteristics	Infants Born to Women with SLE N= 1,274		Infants Born to Women without SLE N= 5,553	
	N	% *	N	% *
<hr/>				
Infant Breastfed during Birth Hospitalization^a				
No	96	13.3	228	7.9
Yes	579	80.3	2,676	92.2
Birthweight (grams)				
<1500	58	4.6	44	0.8
1500–2499	214	16.8	194	3.5
2500–3999	935	73.4	4,625	83.5
4000	60	4.7	673	12.2
Gestational Age at Birth (weeks)				
<28	19	1.5	7	0.1
28– <32	35	2.8	40	0.7
32– <37	240	18.8	294	5.3
37– <42	928	72.8	4,884	91.9
>= 42	5	0.4	92	1.7

^a BMI, Group B Strep, and infant breastfeeding data available from 2003–2013 only; mothers with SLE: n= 723; mothers without SLE: n= 3,060 (except infant breastfeeding; infants of SLE mothers: n= 721, infants of mothers without SLE: n= 3,038).

* Missing data not shown, but percent of total N or total as per footnote a.

Infection-related outcomes during the delivery hospitalization among women with and without systemic lupus erythematosus (SLE), Washington State, 1987–2013

Table 2

Outcome	Women with SLE N=1,1297		Women without SLE N=5,584		RR ^a (95% CI)
	n/total	%	n/total	%	
Any infection	181/1297	14.0	470/5584	8.4	1.7 (1.4, 2.0)
Vaginal births	98/813	12.1	289/4,263	6.8	1.8 (1.5, 2.3)
Cesarean section	83/484	17.2	181/1319	13.7	1.3 (1.0, 1.6)
Received antibiotics^b	225/744	30.2	698/2989	23.4	1.3 (1.1, 1.5)
Vaginal birth	120/406	29.6	463/2,150	21.5	1.4 (1.2, 1.6)
Cesarean section	95/297	32.0	235/839	28.0	1.1 (0.9, 1.4)
Chorioamnionitis	13/1297	1.0	72/5584	1.3	0.8 (0.4, 1.4)

^a Adjusted for maternal age

^b Data available for years 2003–2013 only

Infection-related outcomes in live-born infants of women with and without systemic lupus erythematosus (SLE), Washington State, 1987–2013

Table 3

Outcome	Women with SLE N=1,227		Women without SLE N=5,317		RR ^a (95% CI)	aRR ^{ab} (95% CI)
	n/total	%	n/total	%		
Any infection during birth hospitalization	40/1,227	3.3	69/5,317	1.3	2.6 (1.8, 3.8) *	1.4 (0.9, 2.1)
Term infants (≥ 37 weeks)	11/933	1.2	45/4,975	0.9	1.4 (0.7, 2.7)	--
Pre-term infants (<37 weeks)	29/294	9.9	24/341	7.0	1.4 (0.8, 2.4)	
Received sepsis antibiotics [‡]	23/689	3.3	47/2,950	1.6	2.2 (1.3, 3.5) *	1.3 (0.7, 2.2)
Infection-associated readmission < 30 days	9/1,227	0.7	53/5,317	1.0	0.8 (0.4, 1.6)	0.8 (0.4, 1.7)
Neonatal infection	48/1,227	3.9	120/5,317	2.3	1.8 (1.3, 2.6) *	1.2 (0.8, 1.7)
Neonatal sepsis	27/1,227	2.2	58/5,317	1.1	2.3 (1.4, 3.6) *	1.2 (0.7, 2.0)
NICU admission (maternal smoking) ^c	25/63	39.7	18/274	6.6	6.6 (3.6, 12.0) *	3.3 (1.8, 6.1) *
Limited to term infants (≥ 37 weeks)	9/42	21.4	12/254	4.7	4.7 (1.8, 11.8) *	--
Limited to non-LBW (< 2,500g)	5/42	11.9	13/259	5.0	2.6 (0.9, 7.5)	2.1 (0.8, 5.5)
NICU (maternal non-smoking) ^c	88/621	13.7	145/2,658	5.5	2.6 (2.0, 3.3) *	1.3 (1.0, 1.6) *

^a All outcomes adjusted for maternal age^b Adjusted for gestational age^c Data available for years 2003–2013.

* p<0.05