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## Adverse Perinatal Outcomes Before and After Diagnosis with Systemic Lupus Erythematosus Among African American Women

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### Abstract

**Objective:** Women with systemic lupus erythematosus (SLE) may experience adverse perinatal outcomes in the years before an SLE diagnosis. Overall, there is limited research on perinatal outcomes among African American women with SLE.

**Methods:** Women with SLE identified from the Georgia Lupus Registry and the Georgians Organized Against Lupus Cohort were linked with birth certificates by the Georgia Department of Public Health. Births were categorized into occurring more than 3 years before SLE diagnosis, 0-3 years before SLE diagnosis, 0-3 years after SLE diagnosis or more than 3 years after SLE diagnosis. Comparison births certificates to African American women in the same geographic area were obtained from the National Center for Health Statistics. We used log-risk models to compare the risk of preterm birth or small-for-gestational age among SLE births in each diagnosis timing category to the general population, adjusting for maternal age and education and parity.

**Results:** Births to women with SLE were more likely to occur preterm 0-3 years before SLE diagnosis (risk ratio [RR]: 1.71, 95% confidence interval [CI]: 1.24, 2.35), 0-3 years after SLE diagnosis (RR: 2.29, 95% CI: 1.70, 3.09) and 3 or more years after diagnosis (RR: 2.83, 95% CI: 2.36, 3.38), but not 3 or more years before SLE diagnosis compared to the general population (RR: 1.03, 95% CI: 0.77, 1.38). Similar results were observed for small-for-gestational age births.

**Conclusion:** Our analysis, conducted among African American women, demonstrates an increased risk of adverse perinatal outcomes even before a clinical diagnosis of SLE.

## INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease that commonly affects the heart, skin, joints, kidneys and eyes, and can cause progressive, permanent damage to these organs [1, 2]. The disease is characterized by periods of quiescence, and periods of flare-ups where autoimmune functioning is highly active [3]. Individuals who will be diagnosed with SLE can exhibit autoimmune abnormalities three years before the clinical onset of SLE [4, 5].

Women are nine times as likely to be diagnosed with SLE compared to men, and among women, the incidence among African American women is 3 times the incidence compared to white women [6–8]. As SLE is primarily diagnosed among women, and is typically diagnosed during their reproductive years, understanding the effect of SLE on perinatal outcomes is important [9]. Studies suggest that preterm birth, small-for-gestational age, preeclampsia, fetal and maternal death are all more common among women with SLE than women without SLE [10–16].

While the risk of extreme outcomes such as fetal and maternal mortality are low among women with SLE, the high risk of more common outcomes, such as preterm birth (25–30% of SLE pregnancies among white women) remains concerning [13, 15–17]. Several studies have examined racial disparities in perinatal outcomes between African American and white women with SLE. These studies often had few African American participants and therefore examined composite adverse outcomes or used hospital discharge data to examine ICD-9 codes for preterm labor as a proxy for preterm birth [18–21]. Only one study was large enough to provide estimates for preterm birth, but not small-for-gestational age among African American women with SLE [22]. Small-for-gestational age (SGA) is used as a population-level proxy of fetal growth restriction, which is measured by successive ultrasounds in utero [23]. The estimates for small-for-gestational age are less consistent in SLE pregnancies, but some indicate the risk of small-for-gestational age is nearly 20% among SLE births to white women, while there are no estimates specifically among African American women [11, 13]. Infants born preterm or small-for-gestational age are vulnerable to infant respiratory issues, infection, slow weight gain, stunted growth and impaired cognitive development [23, 24]. Several studies have suggested that there is an elevated risk of adverse perinatal outcomes among women with SLE even before their clinical diagnosis [13, 17, 22, 25, 26].

Despite the interest in pregnancy outcomes among women with SLE, important gaps in the literature remain. There is limited research on preterm birth and SGA specifically among African American women with SLE, and only one study has examined perinatal outcomes before SLE diagnosis among African American women. In the present analysis, we examine the risk of preterm and small-for-gestational age birth among African American women with SLE compared to the general population of African American women in a large metropolitan area. We examine births both before and after the date of SLE diagnosis. We hypothesize that compared to the general African American population, the risk of preterm and SGA births is elevated among African American women with SLE before diagnosis, and elevated to an even greater extent after diagnosis.

## METHODS

### Study Population with Systemic Lupus Erythematosus

Women with SLE were identified from both the Georgia Lupus Registry (GLR) and the Georgians Organized Against Lupus (GOAL) Cohort. The GLR is a population-based registry of individuals living with SLE in 2002-2004 in Fulton and DeKalb counties, the two most populous counties in metropolitan Atlanta, Georgia. Both incident and prevalent cases were identified during this time period. SLE cases were primarily identified from hospitals and rheumatology, nephrology and dermatology groups in and around the catchment area. Administrative databases were also queried retrospectively. To be considered a case, individuals had to either meet 4 of the revised American College of Rheumatology (ACR) Criteria or 3 of the ACR criteria and have a diagnosis of SLE by a board-certified rheumatologist documented in the medical record [6, 27]. The GLR and GOAL were both approved by the Institutional Review Boards of Emory University and the Georgia Department of Public Health.

The GOAL Cohort is an ongoing cohort that originally began recruitment from the GLR, and has since enrolled additional patients with SLE using the same case definition as the GLR from hospitals and clinics in the Atlanta area. Reflecting the racial distribution of SLE in the Atlanta metropolitan area, about 80% of the participants in both GLR/GOAL are African American [6, 28]. This analysis is restricted to African American female participants in GLR/GOAL to generate reliable estimates for an understudied group of women affected by SLE. This analysis was also restricted to singleton births.

Female participants in GLR/GOAL were linked to Georgia birth certificates from 1994 – 2018 on which they are identified as the mother. The data linkage was conducted by the Georgia Department of Public Health with a multi-stage matching algorithm using combinations of various identifying keys [29].

### Comparison Birth Certificates

Birth certificates from the general population between 1994 and 2018 were obtained from the National Center for Health Statistics. All singleton births occurring to African American women in Georgia during the appropriate time frame were identified. Sampling was done to achieve a 1:20 ratio of SLE births to general population births. The sampling of births to the general population was conducted so that the distribution of general population births by year (1994 – 2018) and maternal county of residence matched the distribution of births to women with SLE to generate a more appropriate comparison group.

### Variable Definitions

The exposure of interest was a diagnosis of systemic lupus erythematosus. In GLR/GOAL, a diagnosis of SLE was confirmed by physician review of medical records. When available in GLR/GOAL, the date of diagnosis was captured in medical records. When the medical records were not available, the date of diagnosis was obtained by self-report. Births to women with SLE were categorized as occurring more than three years before diagnosis, within 3 years before diagnosis, within 3 years after diagnosis or more than three years after

diagnosis. Women whose diagnoses occurred during pregnancy were categorized as having their births within 3 years after diagnosis.

Preterm birth was defined as a birth occurring before 37 completed weeks of gestation, identified from the clinical best estimate of gestation on the birth certificate. Small-for-gestational-age births were infants born with birthweights below the 10<sup>th</sup> percentile by gestational age at birth. We used published standards of birthweights by gestational age that were developed from a national dataset of singleton births to non-Hispanic African American mothers [30].

Potential confounders of interest, including maternal age, education, parity and initiation of prenatal care, were obtained from the birth certificate.

### Statistical Analysis

Descriptive characteristics of births in each exposure category were summarized using frequencies and percentages. We generated estimated risk ratios using log-risk models. In our data, births to women with SLE have unique identifiers, where we can identify births occurring to the same woman among women with SLE, but in the set of births to the general population, we cannot identify unique women in the data. Since our main analyses were conducted treating all births as independent events, the precision of the confidence intervals for our estimates is potentially overestimated. We addressed this issue in two ways. First, we conducted a sensitivity analysis that restricted the study population to first births. Second, we conducted a simulation to examine the effect of not accounting for covariance among births in the main analysis. This simulation is described and presented in the Supplementary Appendix S1. We also ran a sensitivity analysis restricting the sample to vaginal births only. Finally, as management of SLE and counseling around pregnancy may have changed between 1994 and 2018, we also ran a final model that included a variable for time period (1994 -2000, 2001 – 2005, 2006 – 2010 or 2011 – 2018), to examine how temporal changes may have affected our results. All analyses were conducted using SAS 9.4 (SAS Institute, Cary, N.C.).

## RESULTS

Our final analytical sample included 583 births to African American women with SLE and 11,660 births to African American women in the general population from metropolitan Atlanta. Among women with SLE, the majority of births occurred before SLE diagnosis, with the greatest proportion (40.8%) occurring more than three years before diagnosis (Table 1). The distribution of maternal age at delivery was slightly younger among African American women with SLE compared to the general population of African American women, with 51.3% of SLE births to women under age 25, compared to 46.0% of births in the general population. Women with SLE were likely to initiate prenatal care in the first trimester (72.2% of births), which was similar to the general population (69.7%). About 40% of SLE births and of births in the general population were first births. A noticeably higher proportion of SLE births were delivered by cesarean section (33.1% vs. 24.7%).

Overall, 28.5% of births in our cohort of African American women with SLE were preterm, compared to 15.5% among African American women in the general population. The proportion of births that were preterm among women with SLE increased linearly by timing of the birth in relation to SLE diagnosis, ranging from 16.4% of births more than three years before diagnosis to 43.3% of births more than 3 years after diagnosis (Figure 1). The pattern was different when examining SGA births. The risk of SGA birth was 10.9% more than three years before diagnosis, but 27.9% within 3 years after diagnosis. By more than three years after SLE diagnosis, the proportion of births that were SGA was 21.3% of births. There also was a trend in the proportion of SLE births that were delivered by cesarean section. Births occurring before SLE diagnosis were about as likely to be delivered by cesarean section as the general population (24.7%), but births occurring within 3 years after diagnosis and more than 3 years after diagnosis were much more likely to be delivered by cesarean section (45.6% and 44.7%) (Figure 2). Preterm births to African American women with SLE were more likely to be delivered by cesarean section than preterm births to women without SLE, especially within 3 years after diagnosis where over 70% of preterm deliveries were by cesarean section, compared to 29% in the general population (Figure 3).

In models adjusted for maternal age, education and parity, births occurring to African American women with SLE more than 3 years before their diagnosis did not have an increased risk of preterm birth compared to the general population (RR: 1.03, 95% CI: 0.77, 1.38) (Table 2). Births occurring within 3 years before diagnosis did have an increased risk of preterm birth compared to the general population (RR: 1.71, 95% CI: 1.24, 2.35). For births to women with SLE occurring after their diagnosis, the risk of preterm birth was more than twice that of the general population. Births more than three years after diagnosis had the highest risk of preterm birth, with a risk ratio of 2.83 (95% CI: 2.36, 3.38). These estimates differed only slightly from the unadjusted estimates.

When we restricted the preterm birth models to first births only (and adjusted for maternal age and education), the estimates showed a similar pattern. SLE was not associated with preterm birth more than 3 years before diagnosis (RR: 1.20, 95% CI: 0.77, 1.86), but the relative risk increased for each diagnosis timing category (within 3 years before, within 3 years after, more than 3 years after), with the greatest relative risk occurring among births more than 3 years after diagnosis (RR: 3.56, 95% CI: 2.74, 4.62). The results were also similar when we restricted to vaginal births only. The estimates from the fully adjusted model for preterm birth did not significantly change after adjusting for time period (results not shown).

In models adjusted for maternal age, education and parity examining the risk of SGA birth, among births to women with SLE more than three years before diagnosis, there was no evidence of an increased risk of SGA birth compared to the general population of African American women (RR: 1.05, 95% CI: 0.72, 1.53) (Table 3). Among births to women with SLE occurring within 3 years before diagnosis, the relative risk increased to 2.38 (95% CI: 1.69, 3.36), and to a maximum of 2.89 (95% CI: 2.03, 4.13) when births occurred within 3 years after SLE diagnosis. Although still greater than the general population, the risk of SGA birth was lower among births occurring more than 3 years after diagnosis compared to those occurring closer to the time of SLE diagnosis (RR: 2.28, 95% CI: 1.69, 3.07). The

unadjusted estimates were of a similar magnitude and showed the same pattern, with the greatest increased risk among SLE births occurring within 3 years after diagnosis.

We also restricted the adjusted model for SGA to first births only. There was a similar pattern among first births. There does not appear to be an association among women more than 3 years before their SLE diagnosis (RR: 0.85, 95%: 0.47, 1.55), but an increase within 3 years before diagnosis (RR: 2.60, 95%: 1.70, 3.99), the greatest increase in risk observed among births occurring within 3 years after SLE diagnosis (RR: 2.96, 95%: 1.74, 5.03), which then decreased more than three years after diagnosis (RR: 2.15, 95%: 1.37, 3.36). The estimates showed a similar pattern when we restricted the model to vaginal births only. The estimates from the fully adjusted model for SGA birth also did not significantly change after adjusting for time period (results not shown).

The results of the simulation analysis presented in the Supplementary Appendix S1 suggest that the precision of the estimated confidence intervals may have been slightly overestimated, by 3-4%, by not accounting for the covariance of births occurring to the same woman (Supplementary Figure S1, Supplementary Figure S2).

## DISCUSSION

The births to African American women with SLE in our study population occurred to slightly younger women than births to the general population of African American women. Births to women with SLE were roughly equally likely to have been to women with a college degree and to be first births compared to the general population of African American women. In our analysis, we found an increased risk of preterm birth and SGA birth among African American women with SLE, both in the years immediately before diagnosis of SLE and in the years after diagnosis. However, we saw a different pattern for preterm births compared to SGA births. The risk of preterm birth was elevated among births occurring within 3 years before diagnosis, 3 years after diagnosis and among births occurring more than three years after diagnosis. The greatest increased risk of SGA occurred in the three years immediately after SLE diagnosis.

Individuals with SLE demonstrate immune abnormalities prior to SLE diagnosis, but perinatal outcomes before diagnosis are not often considered. We could only find five studies that examined perinatal outcomes both before and after SLE diagnosis that also included a comparison group [13, 17, 22, 25, 26]. Two of these studies are from the early 1990's, and may not reflect current practices in counseling SLE pregnancies. Only two used statistical modeling to control for potential confounders. With the exception of Barnado et al., none of these studies provide estimates specifically among African American women. We provide an important replication of Barnado et al.'s findings in a population of African American women in a major metropolitan setting as well as extend their findings to include SGA estimates among African American women with SLE.

All five studies that examined the risk of preterm and/or SGA birth before diagnosis found an increased risk of preterm birth and SGA birth before diagnosis when comparing to a non-SLE cohort. Only one of these studies, Arkema et al., distinguished between births

occurring 2-5 years before diagnosis and 0-2 years before diagnosis in a Swedish cohort. This study found the risks of preterm and SGA births were especially elevated 0-2 years before diagnosis. Our results also provide support for an association between a pre-diagnosis state of SLE and adverse perinatal outcomes among African American women who will eventually be diagnosed with SLE. This could be due to immune abnormalities experienced in the years before a clinical diagnosis. Antiphospholipid antibodies and anti-Ro antibodies can both be elevated years before a clinical SLE diagnosis is possible, and have also been shown to be associated with preterm birth [5, 16, 20]. Conversely, the observed association could be due to the symptoms of active SLE, which have been shown to be associated with adverse perinatal outcomes [31–33]. Diagnosis of SLE is often delayed even after the presentation of clinical symptoms [34].

We could only find one other study that examined the risk of preterm birth before diagnosis specifically among African American women with SLE [22]. Our results were of a similar magnitude as Barnado et al. for births before SLE diagnosis, where they found an odds ratio of 1.87 (95% CI: 1.07, 3.28) for preterm birth, but were less extreme than their results for births after SLE diagnosis, where they found an odds ratio of 4.70 (95% CI: 2.42, 9.13) for preterm birth. Barnado et al. was conducted among Gullah American Americans (220 women with SLE, 217 women without SLE) in the Sea Islands of South Carolina, and the large odds ratio for preterm birth after diagnosis was driven by the low risk of preterm birth in their comparison population, where less than 5% of births were preterm. This low risk of preterm birth is not reflective of the risk of preterm birth among African American women in metropolitan Atlanta (16%), or African American women nationally (14%) [35]. Barnado et al. did not examine SGA births.

We found no other studies that separated births after SLE diagnosis into births occurring in the years immediately following diagnosis and births later after diagnosis, so we cannot compare the differing trend that we saw where the risk of SGA births eventually decreased in the 3 years after SLE diagnosis while preterm births continued to increase. The differing trends may be due to random variability of the data. Conversely, the difference may be due to real factors. While estimates vary, a large proportion of preterm births among women with SLE appear to be medically-indicated, with preeclampsia being a major indicator for preterm delivery [36–38]. Although preeclampsia may result in medically indicated preterm birth, it does not necessarily affect fetal growth. Other aspects of SLE disease that could affect fetal growth may be more likely to be stabilized more than 3 years after diagnosis, resulting in a lower risk of SGA. We could not distinguish between medically-indicated and spontaneous preterm births in our data, but we did have information on method of delivery from the birth certificate. Studies suggest that medically indicated preterm births are more likely to be delivered via cesarean section, while spontaneous preterm births are more likely to be delivered vaginally [36, 39]. In our sample, from within 3 years after diagnosis to 3 or more years after diagnosis, the proportion of preterm births delivered by cesarean section, while decreasing slightly, remained high, going from 71% to 59%. While method of delivery is only a rough proxy for the medical necessity of a preterm delivery, this suggests that spontaneous and medically-indicated preterm births remain common, even after a stable treatment regimen for SLE may be established in the early years after diagnosis.

Some limitations should be noted. In Georgia insurance status and maternal receipt of WIC were only available on the birth certificate beginning in 2009 which would have rendered our sample size too small to conduct a multivariable analysis. Data on hypertension and diabetes available on birth certificates is known to be of poor quality, and substantially underestimates the proportion of births to women affected by these conditions [40, 41]. We therefore chose to not include these variables in our analysis. We also did not have data on SLE disease activity or medications during pregnancy. We used birth certificates from the general population of African American women in Georgia as our comparison group. This set of comparison birth certificates potentially contained births to women with SLE, and we have no way to exclude these births using information from the birth certificate. The estimated prevalence of SLE among African American women in Georgia is 196.2 per 100,000 [6]. With the age distribution of the 11,660 African American women included in our comparison group, the expected prevalence of SLE in our comparison group is approximately 0.20%, or 22 women. We do not expect this to have influenced our results. We also did not have a unique identifier among the comparison births to identify births to the same woman. Our simulation analysis (Supplementary Appendix S1) demonstrated that not accounting for births to the same women likely generated estimated confidence intervals that were only 3-4% narrower than what would have been estimated had we been able to account for the covariance of multiple births to the same woman. Finally, as previously mentioned, we were unable to differentiate between medically-indicated and spontaneous preterm births.

Our analysis has several strengths. We included only validated cases of SLE. Studies that draw patients from administrative databases identify women with SLE by the presence of the International Classification of Diseases (ICD)-9 code 710.0 in discharge records [10, 12, 21, 38, 42, 43]. In studies that have validated the use of the ICD code against medical record abstraction in the general population, the positive predictive value of the ICD code alone was approximately 60%, suggesting that a number of SLE cases identified by the code are not true cases [44]. We also included births to women with SLE both before and after clinical diagnosis and were able to demonstrate that the risks for both preterm birth and SGA are elevated in the years before diagnosis. Finally, our study included a large sample of self-identified African American women with SLE, who have been understudied with respect to perinatal outcomes, yet represent a group at a high risk of SLE.

As the prognosis for women diagnosed with SLE improves, more women with SLE will likely pursue pregnancy and childbearing. Our results suggest that African American women with SLE are at greater risk for the adverse outcomes preterm birth and SGA than the general population of African American women, even before a clinical diagnosis of SLE. In general, African American women have a higher risk of preterm birth and SGA, a greater risk of pregnancy complications that may lead to these outcomes, including preeclampsia and gestational hypertension, and are more likely to die in childbirth than white women [45–48]. More work remains to be done to characterize the additional risks around pregnancy and childbirth that African American women with SLE face. Healthcare providers, especially those in communities of color should be better educated about SLE, and have a lower threshold to suspect SLE in the peripartum period.



## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

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## REFERENCES

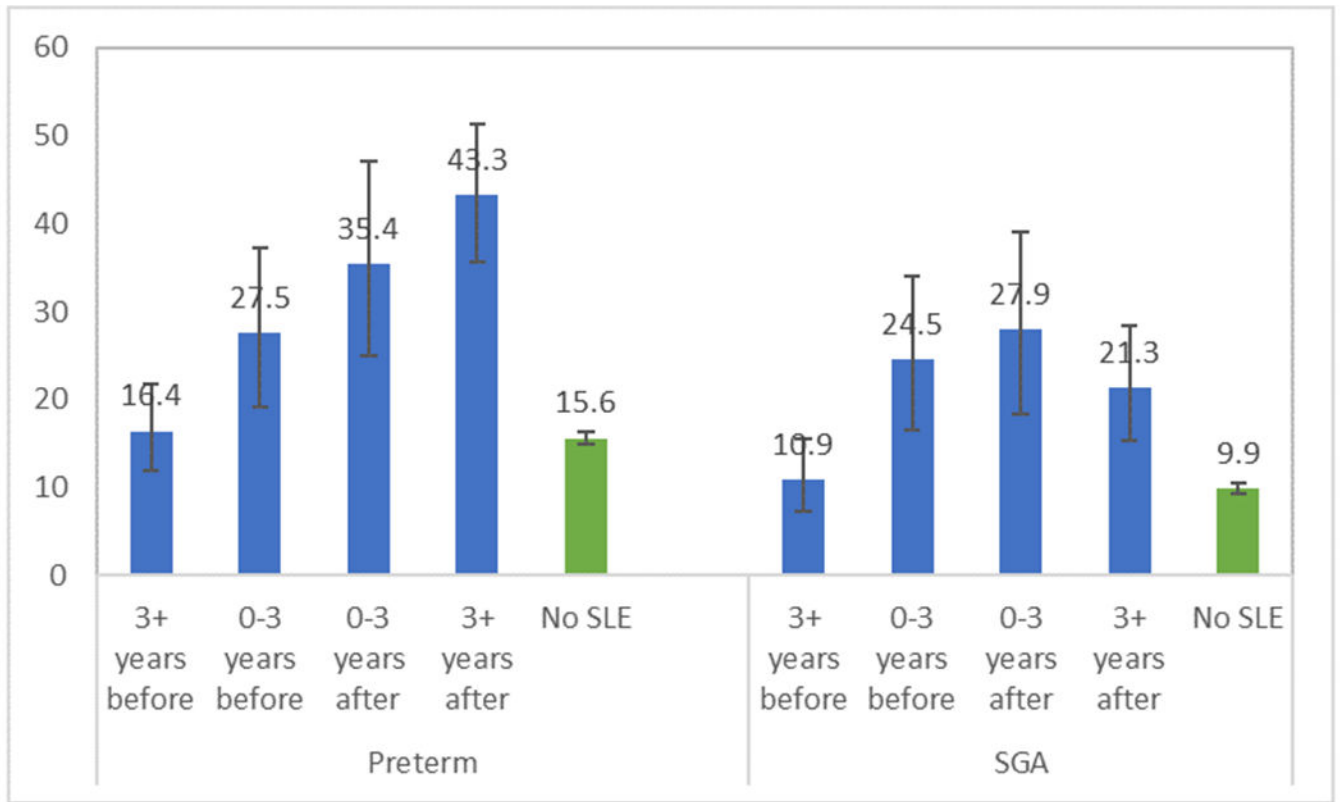
1. Tsokos GC, Systemic lupus erythematosus. *N Engl J Med*, 2011. 365(22): p. 2110–21. [PubMed: 22129255]
2. Taraborelli M, et al. , Organ damage accrual and distribution in systemic lupus erythematosus patients followed-up for more than 10 years. *Lupus*, 2017. 26(11): p. 1197–1204. [PubMed: 28420047]
3. Ines L, et al. , Identification of clinical predictors of flare in systemic lupus erythematosus patients: a 24-month prospective cohort study. *Rheumatology (Oxford)*, 2014. 53(1): p. 85–9. [PubMed: 24067885]
4. Arbuckle MR, et al. , Development of anti-dsDNA autoantibodies prior to clinical diagnosis of systemic lupus erythematosus. *Scand J Immunol*, 2001. 54(1-2): p. 211–9. [PubMed: 11439169]
5. Arbuckle MR, et al. , Development of autoantibodies before the clinical onset of systemic lupus erythematosus. *N Engl J Med*, 2003. 349(16): p. 1526–33. [PubMed: 14561795]
6. Lim SS, et al. , The incidence and prevalence of systemic lupus erythematosus, 2002-2004: The Georgia Lupus Registry. *Arthritis Rheumatol*, 2014. 66(2): p. 357–68. [PubMed: 24504808]
7. Dall’Era M, et al. , The Incidence and Prevalence of Systemic Lupus Erythematosus in San Francisco County, California: The California Lupus Surveillance Project. *Arthritis Rheumatol*, 2017. 69(10): p. 1996–2005. [PubMed: 28891237]
8. Izmirly PM, et al. , The Incidence and Prevalence of Systemic Lupus Erythematosus in New York County (Manhattan), New York: The Manhattan Lupus Surveillance Program. *Arthritis Rheumatol*, 2017. 69(10): p. 2006–2017. [PubMed: 28891252]
9. Pons-Estel GJ, et al. , Understanding the epidemiology and progression of systemic lupus erythematosus. *Semin Arthritis Rheum*, 2010. 39(4): p. 257–68. [PubMed: 19136143]
10. Ling N, Lawson E, and von Scheven E, Adverse pregnancy outcomes in adolescents and young women with systemic lupus erythematosus: a national estimate. *Pediatr Rheumatol Online J*, 2018. 16(1): p. 26. [PubMed: 29661199]
11. Kroese SJ, et al. , Maternal and Perinatal Outcome in Women with Systemic Lupus Erythematosus: A Retrospective Bicenter Cohort Study. *J Immunol Res*, 2017. 2017: p. 8245879. [PubMed: 29094052]
12. Clowse ME, et al. , A national study of the complications of lupus in pregnancy. *Am J Obstet Gynecol*, 2008. 199(2): p. 127 e1-6. [PubMed: 18456233]
13. Arkema EV, et al. , What to Expect When Expecting With Systemic Lupus Erythematosus (SLE): A Population-Based Study of Maternal and Fetal Outcomes in SLE and Pre-SLE. *Arthritis Care Res (Hoboken)*, 2016. 68(7): p. 988–94. [PubMed: 27338103]
14. Nili F, et al. , Maternal and neonatal outcomes in pregnancies complicated by systemic lupus erythematosus: a population-based study. *J Obstet Gynaecol Can*, 2013. 35(4): p. 323–328. [PubMed: 23660039]
15. Jakobsen IM, Helmgig RB, and Stengaard-Pedersen K, Maternal and foetal outcomes in pregnant systemic lupus erythematosus patients: an incident cohort from a stable referral population followed during 1990-2010. *Scand J Rheumatol*, 2015. 44(5): p. 377–84. [PubMed: 26087812]
16. Al Arfaj AS and Khalil N, Pregnancy outcome in 396 pregnancies in patients with SLE in Saudi Arabia. *Lupus*, 2010. 19(14): p. 1665–73. [PubMed: 20947541]

17. Petri M and Allbritton J, Fetal outcome of lupus pregnancy: a retrospective case-control study of the Hopkins Lupus Cohort. *J Rheumatol*, 1993. 20(4): p. 650–6. [PubMed: 8496859]
18. Kaplowitz ET, et al. , Contribution of Socioeconomic Status to Racial/Ethnic Disparities in Adverse Pregnancy Outcomes Among Women With Systemic Lupus Erythematosus. *Arthritis Care Res (Hoboken)*, 2018. 70(2): p. 230–235. [PubMed: 28480528]
19. Andrade R, et al. . Adverse pregnancy outcomes in women with systemic lupus erythematosus from a multiethnic US cohort: LUMINA (LVI) [corrected]. *Clin Exp Rheumatol*, 2008. 26(2): p. 268–74. [PubMed: 18565248]
20. Buyon JP, et al. , Predictors of Pregnancy Outcomes in Patients With Lupus: A Cohort Study. *Ann Intern Med*, 2015. 163(3): p. 153–63. [PubMed: 26098843]
21. Clowse ME and Grotegut C, Racial and Ethnic Disparities in the Pregnancies of Women With Systemic Lupus Erythematosus. *Arthritis Care Res (Hoboken)*, 2016. 68(10): p. 1567–72. [PubMed: 26815791]
22. Barnado A, et al. , Pregnancy outcomes among African-American patients with systemic lupus erythematosus compared with controls. *Lupus Sci Med*, 2014. 1(1): p. e000020. [PubMed: 25360323]
23. Sharma D, et al. , Intrauterine growth restriction - part 2. *J Matern Fetal Neonatal Med*, 2016. 29(24): p. 4037–48. [PubMed: 26979578]
24. Platt MJ, Outcomes in preterm infants. *Public Health*, 2014. 128(5): p. 399–403. [PubMed: 24794180]
25. Julkunen H, et al. , Fetal outcome in lupus pregnancy: a retrospective case-control study of 242 pregnancies in 112 patients. *Lupus*, 1993. 2(2): p. 125–31. [PubMed: 8330034]
26. Dhar JP, et al. , Pregnancy outcomes before and after a diagnosis of systemic lupus erythematosus. *Am J Obstet Gynecol*, 2005. 193(4): p. 1444–55. [PubMed: 16202739]
27. 1997 Update of the 1982 American College of Rheumatology Revised Criteria for Classification of Systemic Lupus Erythematosus. 1997 [cited 2018 October 3, 2018]; Available from: <https://www.rheumatology.org/Portals/0/Files/1997%20Update%20of%201982%20Revised.pdf>.
28. Drenkard C, et al. , Primary preventive services in patients with systemic lupus erythematosus: study from a population-based sample in Southeast U.S. *Semin Arthritis Rheum*, 2013. 43(2): p. 209–16. [PubMed: 23731530]
29. Ido MS, et al. , Administrative data linkage to evaluate a quality improvement program in acute stroke care, Georgia, 2006-2009. *Prev Chronic Dis*, 2015. 12: p. E05. [PubMed: 25590599]
30. Oken E, et al. , A nearly continuous measure of birth weight for gestational age using a United States national reference. *BMC Pediatr*, 2003. 3: p. 6. [PubMed: 12848901]
31. Clowse ME, et al. , Predictors of preterm birth in patients with mild systemic lupus erythematosus. *Ann Rheum Dis*, 2013. 72(9): p. 1536–9. [PubMed: 23361085]
32. Palma Dos Reis CR, et al. , Prediction of Adverse Pregnancy Outcomes in Women with Systemic Lupus Erythematosus. *Clin Rev Allergy Immunol*, 2019.
33. Skorpen CG, et al. , Influence of disease activity and medications on offspring birth weight, preeclampsia and preterm birth in systemic lupus erythematosus: a population-based study. *Ann Rheum Dis*, 2018. 77(2): p. 264–269. [PubMed: 29092851]
34. Rees F, et al. , Early Clinical Features in Systemic Lupus Erythematosus: Can They Be Used to Achieve Earlier Diagnosis? A Risk Prediction Model. *Arthritis Care Res (Hoboken)*, 2017. 69(6): p. 833–841. [PubMed: 27588834]
35. Prevention, C.f.D.C.a. Preterm Birth. 2020 October 30, 2020 [cited 2021 May 2, 2021]; Available from: <https://www.cdc.gov/reproductivehealth/maternalinfanthealth/pretermbirth.htm>.
36. Eudy AM, et al. , Reasons for cesarean and medically indicated deliveries in pregnancies in women with systemic lupus erythematosus. *Lupus*, 2018. 27(3): p. 351–356. [PubMed: 28699378]
37. Chakravarty EF, et al. , Factors that predict prematurity and preeclampsia in pregnancies that are complicated by systemic lupus erythematosus. *American Journal of Obstetrics and Gynecology*, 2005. 192(6): p. 1897–1904. [PubMed: 15970846]
38. Kolstad KD, et al. , Preterm birth phenotypes in women with autoimmune rheumatic diseases: a population-based cohort study. *BJOG*, 2019.

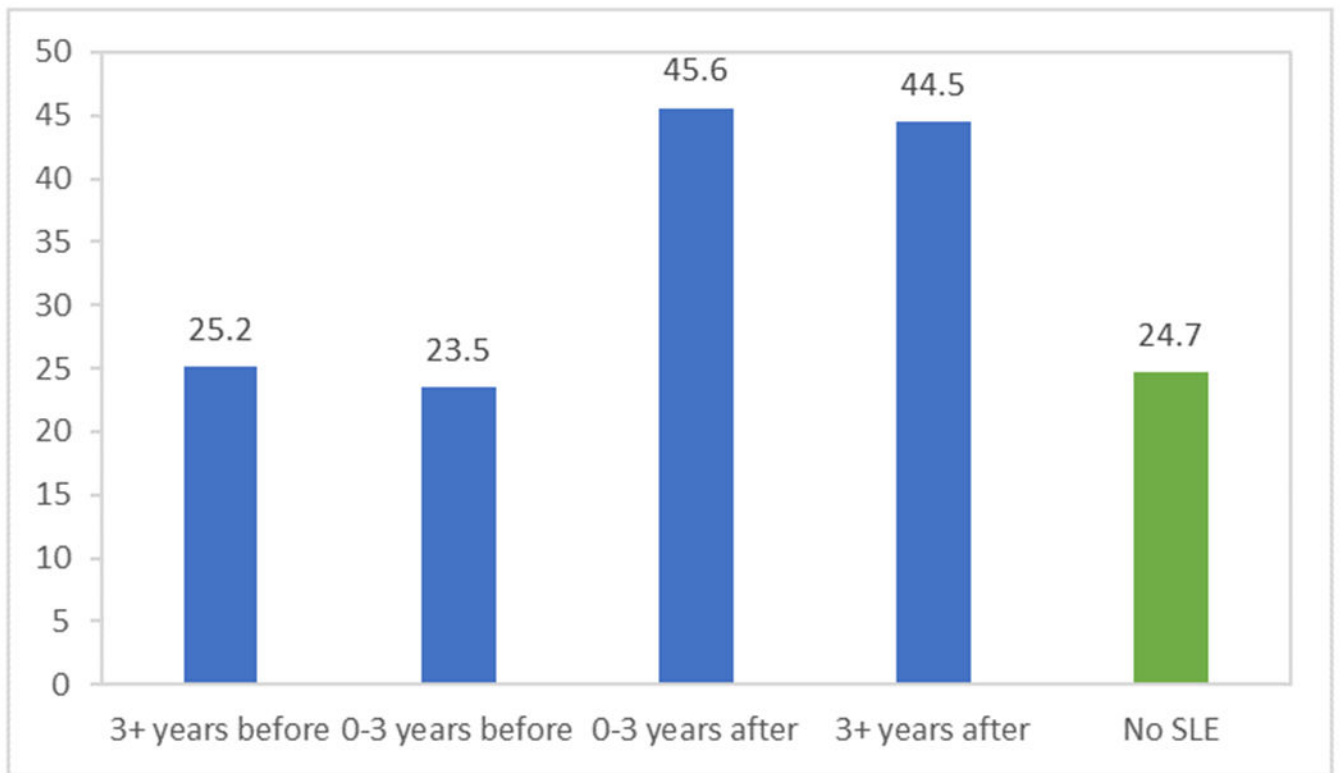
39. Stout MJ, Macones GA, and Tuuli MG, Accuracy of Birth Certificate Data for Classifying Preterm Birth. *Paediatr Perinat Epidemiol*, 2017. 31(3): p. 245–249. [PubMed: 28370345]
40. DiGiuseppe DL, et al. , Reliability of birth certificate data: a multi-hospital comparison to medical records information. *Matern Child Health J*, 2002. 6(3): p. 169–79. [PubMed: 12236664]
41. Lydon-Rochelle MT, et al. , The reporting of pre-existing maternal medical conditions and complications of pregnancy on birth certificates and in hospital discharge data. *Am J Obstet Gynecol*, 2005. 193(1): p. 125–34. [PubMed: 16021070]
42. Mehta B, et al. , Trends in Maternal and Fetal Outcomes Among Pregnant Women With Systemic Lupus Erythematosus in the United States: A Cross-sectional Analysis. *Ann Intern Med*, 2019. 171(3): p. 164–171. [PubMed: 31284305]
43. Williams A, et al. , Obstetric and neonatal complications among women with autoimmune disease. *J Autoimmun*, 2019. 103: p. 102287. [PubMed: 31147159]
44. Moores KG and Sathe NA, A systematic review of validated methods for identifying systemic lupus erythematosus (SLE) using administrative or claims data. *Vaccine*, 2013. 31 Suppl 10: p. K62–73. [PubMed: 24331075]
45. Schaaf JM, et al. , Ethnic and racial disparities in the risk of preterm birth: a systematic review and meta-analysis. *Am J Perinatol*, 2013. 30(6): p. 433–50. [PubMed: 23059494]
46. Grobman WA, et al. , Racial Disparities in Adverse Pregnancy Outcomes and Psychosocial Stress. *Obstet Gynecol*, 2018. 131(2): p. 328–335. [PubMed: 29324613]
47. Force, U.S.P.S.T., et al. , Screening for Preeclampsia: US Preventive Services Task Force Recommendation Statement. *JAMA*, 2017. 317(16): p. 1661–1667. [PubMed: 28444286]
48. Joseph KS, et al. , Maternal Mortality in the United States: Recent Trends, Current Status, and Future Considerations. *Obstet Gynecol*, 2021. 137(5): p. 763–771. [PubMed: 33831914]

### **SIGNIFICANCE AND INNOVATIONS**

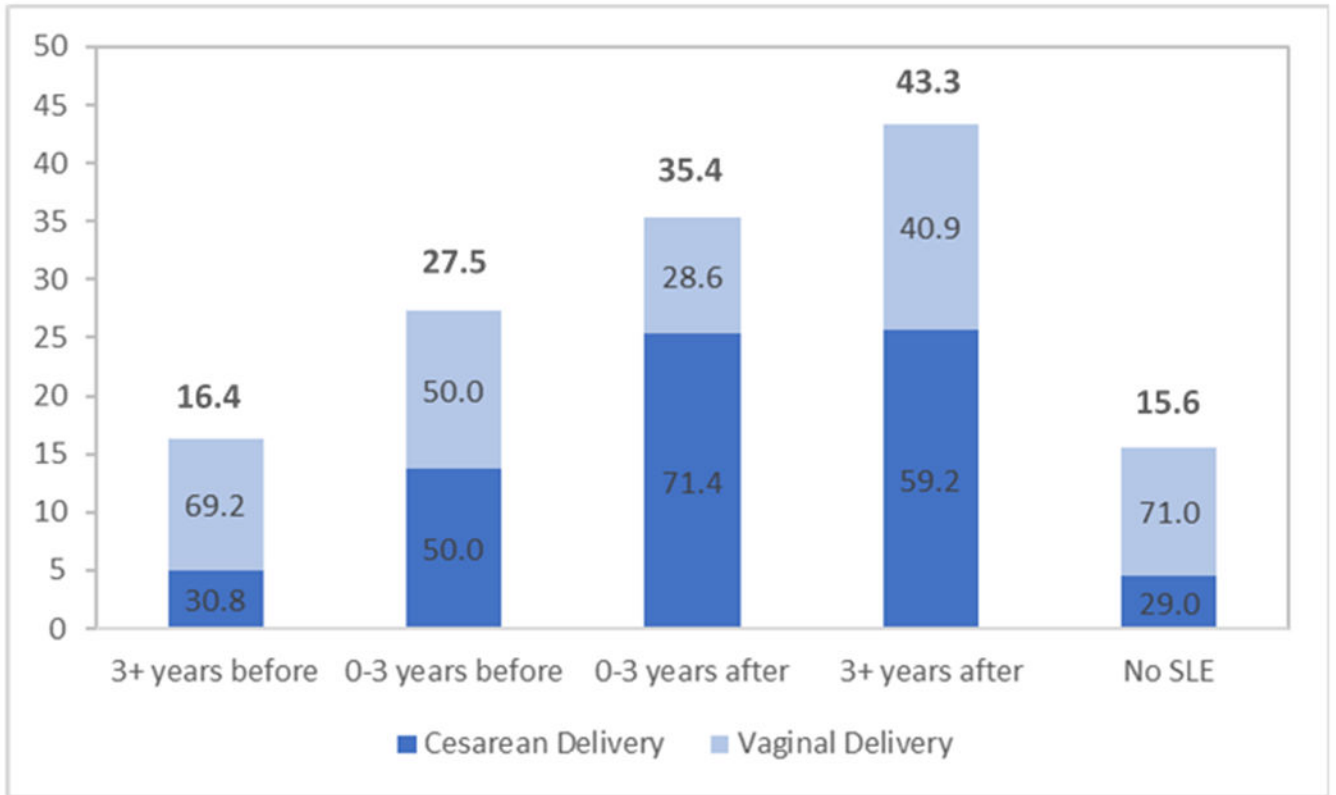
- African American women with SLE are at an increased risk of delivering preterm or small-for-gestational age infants compared to the general population.
- There is an increased risk of delivering preterm or small-for-gestational age infants among African American women in the years before they receive a diagnosis of SLE.



**Figure 1.** Preterm birth and small-for-gestational age by timing of birth in relation to SLE diagnosis among African American women



**Figure 2.** Proportion of births delivered by cesarean section by timing of SLE diagnosis among African American women



**Figure 3.** Delivery method among preterm births to African American women (overall proportion of births that were preterm in bold)

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**Table 1.**

## Participant characteristics

Characteristic	SLE births (N=583)	Non-SLE Births (N=11,660)
Timing of Birth		
>3 years before diagnosis	238 (40.8)	
Within 3 years before diagnosis	102 (17.5)	
Within 3 years after diagnosis	79 (13.6)	
>3 years after diagnosis	164 (28.1)	
Preterm		
Preterm	166 (28.5)	1812 (15.6)
Not preterm	417 (71.5)	9829 (84.4)
Small-for-Gestational Age		
SGA	108 (18.5)	1141 (9.9)
Not SGA	475 (81.5)	10426 (90.1)
Maternal Age		
12-19	119 (20.4)	1949 (16.7)
20-24	180 (30.9)	3411 (29.3)
25-29	138 (23.7)	2934 (25.2)
30-34	90 (15.4)	2082 (17.9)
35-39	44 (7.6)	1050 (9.0)
40+	12 (2.1)	234 (2.0)
Prenatal Care Initiation		
First Trimester	421 (72.2)	8122 (69.7)
Second Trimester	88 (15.1)	1890 (16.2)
Third Trimester	11 (1.9)	389 (3.3)
No Prenatal Care	6 (1.0)	293 (2.5)
Unknown	57 (9.8)	966 (8.3)
Parity		
1	238 (40.8)	4571 (39.3)
2-3	263 (45.1)	5182 (44.6)
4+	82 (14.1)	1879 (16.2)
Delivery Method		
Vaginal	390 (66.9)	8756 (75.3)
Cesarean Section	193 (33.1)	2872 (24.7)
Education		



Characteristic	SLE births (N=583)	Non-SLE Births (N=11,660)
High School or Less	367 (64.2)	6846 (60.1)
Some College	127 (22.2)	2700 (23.7)
College or Higher	78 (13.6)	1841 (16.2)

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**Table 2.**

Risk ratios modeling the risk of preterm birth among African American women

	<b>Unadjusted</b>	<b>Adjusted*</b>	<b>First births only*</b>	<b>Vaginal births only*</b>
3+years before diagnosis	1.05 (0.79, 1.41)	1.03 (0.77, 1.38)	1.20 (0.77, 1.86)	0.99 (0.69, 1.41)
Within 3 years before diagnosis	1.76 (1.28, 2.42)	1.71 (1.24, 2.35)	1.90 (1.19, 3.04)	1.18 (0.73, 1.90)
Within 3 years after diagnosis	2.28 (1.69, 3.08)	2.29 (1.70, 3.09)	2.75 (1.68, 4.49)	1.30 (0.70, 2.43)
3+ years after diagnosis	2.78 (2.32, 3.33)	2.83 (2.36, 3.38)	3.56 (2.74, 4.62)	2.21 (1.62, 3.01)

\* Adjusted for maternal age, education and parity

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**Table 3.**

Risk ratios modeling the risk of small-for-gestational age

	<b>Unadjusted</b>	<b>Adjusted*</b>	<b>First births only*</b>	<b>Vaginal births only*</b>
3+years before diagnosis	1.11 (0.77, 1.60)	1.05 (0.72, 1.53)	0.85 (0.47, 1.55)	0.97 (0.61, 1.53)
Within 3 years before	2.48 (1.76, 3.51)	2.38 (1.69, 3.36)	2.60 (1.70, 3.99)	2.39 (1.61, 3.56)
Within 3 years after	2.82 (1.97, 4.04)	2.89 (2.03, 4.13)	2.96 (1.74, 5.03)	2.88 (1.78, 4.67)
3+ years after	2.16 (1.60, 2.92)	2.28 (1.69, 3.07)	2.15 (1.37, 3.36)	1.44 (0.85, 2.45)

\* Adjusted for maternal age, education and parity

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