



Published in final edited form as:

J Autoimmun. 2019 September ; 103: 102287. doi:10.1016/j.jaut.2019.05.015.

Obstetric and neonatal complications among women with autoimmune disease

Andrew Williams^a, Katherine Grantz^a, Indulaxmi Seeni^a, Candace Robledo^b, Shanshan Li, Scd^c, Marion Ouidir^a, Carrie Nobles^a, Pauline Mendola^{a,*}

^aEpidemiology Branch, Division of Intramural Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, MD, USA

^bDepartment of Population Health and Biostatistics, University of Texas Rio Grande Valley School of Medicine, Harlingen, TX, USA

^cSlone Epidemiology Center, Boston University School of Medicine, Boston, MA, USA

Abstract

Background: The impact of autoimmune diseases on pregnancy remains understudied on a population level. Examination of obstetric and neonatal outcomes among women with autoimmune disease and their infants can provide important insights for clinical management.

Methods: Autoimmune diseases and outcomes were identified using medical records. Cesarean delivery, preterm birth, preeclampsia, small for gestational age (SGA), neonatal intensive care (NICU) admission, neonatal respiratory distress syndrome (RDS), and perinatal mortality risk was assessed. Poisson regression with robust standard errors estimated relative risks (RR) and 95% confidence intervals (95% CI) with adjustment for maternal characteristics and other chronic conditions.

Results: Women with T1DM were at increased risk for nearly all outcomes including RDS (RR: 3.62; 95% CI: 2.84, 4.62), perinatal mortality (RR: 2.35; 95% CI: 1.12, 4.91), cesarean delivery (RR: 2.16; 95% CI: 2.02, 2.32) and preterm birth (RR: 3.52; 95% CI: 3.17, 3.91). Women with SLE also had higher risk for preterm delivery (RR: 2.90; 95% CI: 2.42, 3.48) and RDS (RR: 2.99; 95% CI: 1.99, 4.51) as did women with Crohn's (cesarean delivery RR: 1.31, 95% CI: 1.08, 1.60; preterm delivery RR: 1.84, 95% CI: 1.37, 2.49. RA increased risk for SGA (RR: 1.66; 95% CI: 1.08, 2.55).

Conclusion(s): Despite the heterogeneity in autoimmune diseases, we observed elevated preterm birth risk for most women with autoimmune disease. SLE and T1DM appeared to confer increased risk for a wide range of adverse outcomes.

*Corresponding author. 6710B Rockledge, MSC 7004, Room 3119, Bethesda, MD, 20892, USA. pauline.mendola@nih.gov (P. Mendola).

Conflicts of interest

Authors report no conflict of interest.

This work was previously presented at the American College of Epidemiology 2018 Annual Meeting, University of Cincinnati, Cincinnati, Ohio, September 23–25, 2018.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jaut.2019.05.015>.

Keywords

Type 1 diabetes; Systemic lupus erythematosus; Autoimmune disease; Neonatal; Obstetric

1. Introduction

The worldwide estimated cumulative prevalence of autoimmune disease is approximately 5% [1], and increasing [2]. Approximately 66% of autoimmune diseases have a mean age of onset less than 50 years [1], and 80% of autoimmune cases in the U.S. occur among women [3,4]. It is important to understand the effect autoimmune diseases have on pregnant women and their infants.

The physiologic regulation of inflammation during pregnancy plays an important function in obstetric and neonatal outcomes. Inflammation, an immune-mediated response, assists in implantation and placentation early in pregnancy. Inflammation also promotes parturition and placental expulsion [5]. Later in gestation, pro-inflammatory processes at the maternal/fetal interface due to infection or placental abruption may lead to preterm birth, preeclampsia, and other adverse outcomes [6]. Research into the etiology of these outcomes is warranted. Inflammation is a key feature of autoimmune disease [3,4,7]. However, the population-level impact of autoimmune diseases on pregnancy remains understudied. Our previous work found women with asthma or thyroid disease had an increased risk for poor obstetric and infant outcomes [8–10], yet not all cases of asthma or thyroid disease are autoimmune. The underlying biologic mechanisms linking autoimmune disease and increased risk of adverse obstetric and neonatal outcomes are not well understood yet may result from overlapping physiologic adaptations necessary for pregnancy [11,12], their disease states [13–20], the presence of autoantibodies or medications [21,22] required for management during pregnancy [17,21,23,24].

A challenge in studying the association of autoimmune diseases with obstetric and neonatal outcomes is the rarity of both. Research conducted to date is largely among homogenous populations outside the U.S. [14–17,22,25–41]. Studies conducted among U.S. populations are often limited by small sample sizes [21,30,40] or focused on a specific autoimmune disease and lacked detailed data on multiple obstetric and infant outcomes [34,42,43].

Cesarean delivery and preterm delivery are most frequently examined in the existing literature. Women with type 1 diabetes mellitus (T1DM) [12,32,41,44], systemic lupus erythematosus (SLE) [45–48], Crohn's disease [49–52] or rheumatoid arthritis (RA) [22,53,54] are reported to be at increased risk for cesarean delivery but evidence among women with multiple sclerosis (MS) is mixed. Two population-based studies found women with MS had approximately 40% higher risk for cesarean delivery [27,28], while two other population-based studies [26,55] and two small case-control studies [25,56] found no increased risk. In addition, prior studies did not explore the indications or timing of cesarean deliveries (prelabor or intrapartum).

Similarly, evidence among women with T1DM [14,44], SLE [18,57], Crohn's [52,58,59] or RA [18,31,34] suggests increased risk of preterm birth while reports of preterm birth risk

among women with MS are inconsistent. Two population-based studies report an increased preterm birth risk among women with MS [27,28], and four other studies report no increased risk [25,26,29,30]. No data are available regarding precursors of preterm birth or spontaneous versus induced deliveries among women with autoimmune disease.

Evidence for other prevalent complications associated with autoimmune disease is also inconclusive. For example, among women with RA, four studies report an increased risk of small for gestational age (SGA) [21,31,32,60], while four studies report no increased risk of SGA [16,22,33,34]. Evidence regarding neonatal intensive care unit (NICU) admission is also sparse with mixed results [15–17,22,33,35–40]. For certain autoimmune diseases like T1DM, and Crohn's disease, studies are limited and none have been conducted among US populations [14,15,39,41].

Using a nationwide US cohort, we aimed to provide a more comprehensive description of the obstetric and neonatal risks among women with autoimmune disease and their infants. To better understand obstetric and neonatal risks associated with maternal autoimmune disease, we examined women in the Consortium on Safe Labor (CSL) diagnosed with T1DM, SLE, Crohn's, MS, or RA. These diseases are heterogeneous and their target tissues vary (pancreatic β -cells for T1DM [61]; various tissues including musculoskeletal, renal, and central nervous system for SLE [62]; bowel in Crohn's [63]; the nervous system in MS [64]; and musculoskeletal system in RA [65]).

2. Materials and methods

2.1. Consortium on Safe Labor

The CSL was a U.S. retrospective cohort study from 2002 to 2008 that abstracted labor and delivery information from electronic medical records from 19 U.S. hospitals. Data extracted for deliveries at 23 gestational weeks or later ($n = 228,438$) included: maternal socio-demographic characteristics, medical, reproductive and prenatal history, labor and delivery summaries, postpartum and newborn data [66]. For these analyses, we excluded multifetal pregnancies ($n = 5,063$, 2.2%), mothers with thyroid disease ($n = 3,772$, 1.6%), mothers with other autoimmune disease ($n = 1,764$, 0.7%) such as unspecified diseases of connective tissue, thrombophilia, hemorrhagic conditions, ulcerative colitis, coeliac disease, Grave's disease and Hashimoto's thyroiditis, and participants from one site for which ICD-9 codes were not reported and no cases of the autoimmune diseases of interest were identified ($n = 12,318$, 5.3%). Our final analytic sample included 205,521 deliveries. Institutional Review Boards approval was obtained at all participating sites and data are de-identified.

2.2. Autoimmune diseases of interest

Relatively common maternal autoimmune diseases were selected for analyses in part to ensure sufficient sample size. T1DM, SLE, Crohn's, MS, and RA were identified using delivery admission electronic medical records and discharge ICD-9 codes (Supplementary Table 1). The sensitivity of these codes for obstetric conditions is generally good [66–68]. For women with multiple pregnancies during the study period, a diagnosis of autoimmune

disease was assumed for subsequent pregnancies (52 repeat pregnancies among women with autoimmune disease, 4.5% of pregnancies to women with autoimmune disease).

2.3. Obstetric and neonatal outcomes

Outcome variables were elected based on prevalence and prior studies: cesarean delivery (overall, pre-labor, after induced labor, and after spontaneous labor), preeclampsia, preterm birth (< 37 weeks of gestation; overall, spontaneous preterm delivery, indicated preterm delivery), small for gestational age, NICU admission, neonatal respiratory distress syndrome (RDS), and perinatal mortality (pregnancy loss > 23 weeks of gestation through neonatal mortality < 7 days) were identified from maternal and neonatal medical records supplemented with discharge ICD-9 codes (Supplementary Table 1).

2.4. Statistical analysis

Descriptive statistics were summarized by autoimmune disease status (Present/Absent). Binary Poisson regression models with the log link function and robust standard errors to account for repeat pregnancies estimated relative risks (RR) and 95% confidence intervals (95% CI) for the association between autoimmune disease and out-comes of interest. Women with autoimmune disease and their infants were compared to women without any autoimmune disease. Models were adjusted for maternal age (continuous), maternal race/ethnicity (White, Black, Hispanic, Asian/Pacific Islander, Other), health insurance (public, private, other), marital status (married, divorced/widowed, single, unknown), smoking during pregnancy (yes/no), alcohol use during pregnancy (yes/no), any other chronic diseases (yes/no: type 2 diabetes, asthma, depression, heart disease, hypertension, renal disease) and census region (Northeast, West, South, Midwest), based on previous literature [4,20,22,27,31,41,48,52].

We also compared indications for cesarean delivery and precursors for preterm delivery by autoimmune disease status. All statistical analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, NC, USA). We did not adjust for multiple comparisons [69].

3. Results

3.1. Prevalence of autoimmune diseases

The prevalence of autoimmune diseases (cases per 1000 pregnancies) for the CSL population by demographic variables are presented in Table 1.

Black women had the highest rates of T1DM (2.9/1000) and SLE (1.3/1000), while white women had the highest rates of Crohn's (1.4/1000), MS (1/1000), and RA (0.8/1000). Women with private insurance had the highest rates of SLE (1.1/1000), Crohn's (1.1/1000), and MS (0.9/1000). Women with public insurance had the highest rate of T1DM (2.9/1000). Rates of T1DM, SLE, and Crohn's varied by census region. Rates of T1DM were highest for women in the Midwest (3.1/1000) and the South (2.9/1000). Women in the South had the highest rate of SLE (1.4/1000), and women in the Northeast had the highest rate of Crohn's disease (1.4/1000).

Women with autoimmune disease and their infants generally experienced more adverse outcomes compared to women without autoimmune disease (Tables 2 and 3). Women with any of the examined autoimmune diseases, when compared to women without autoimmune disease, had significantly higher rates of cesarean delivery, pre-labor cesarean delivery, preterm birth, and spontaneous preterm birth. Women with T1DM, SLE, or Crohn's also had higher rates of preeclampsia and indicated preterm birth. Women with T1DM or SLE had similarly high rates of poor obstetric outcomes, except for cesarean delivery, where T1DM was associated with the highest rates (Table 2).

Only women with SLE or RA had significantly higher rates of SGA, while women with T1DM had lower rates of SGA as expected, compared to women without autoimmune disease.

3.2. Risk of adverse obstetric and neonatal outcomes

Results were similar in adjusted analyses (Table 3), with all autoimmune diseases associated with increased risk for cesarean delivery, including for pre-labor cesarean and cesarean after induced or spontaneous labor, and preterm birth, including both indicated and spontaneous preterm birth.

Models adjusted for maternal age, maternal race/ethnicity, preconception body mass index, health insurance, marital status, smoking in pregnancy, alcohol use in pregnancy, other chronic diseases, and census region.; * $p < 0.05$ indicates rates among women with autoimmune disease different than rates among women without autoimmune disease.

Women with T1DM were at increased risk for most poor obstetric outcomes, except for SGA (RR:0.61, 95% CI: 0.43, 0.86). Similarly, women with SLE were at increased risk for most obstetric outcomes.

Infants born to women with autoimmune disease, compared to those born to women without autoimmune disease, appear to have elevated risk for most adverse neonatal outcomes, but many associations did not reach statistical significance (Tables 2 and 3). However, compared to infants born to women without autoimmune disease, infants born to women with T1DM were three times more likely to experience RDS (RR: 3.62; 95% CI: 2.84, 4.62), and twice as likely to experience perinatal mortality (RR: 2.35; 95% CI: 1.12, 4.91), and had a 25% risk of NICU admission (RR: 1.25; 95% CI: 1.16, 1.35). Infants born to women with SLE had similar increases in risk for RDS and NICU admission.

3.3. Intrapartum cesarean delivery and indicated preterm delivery

As risk of cesarean or preterm delivery were increased for women with autoimmune diseases, we examined indications for intrapartum cesarean deliveries (Table 4) and for indicated preterm deliveries (Table 5).

For intrapartum cesarean deliveries (Table 4), failure to progress was the most common indication for women with T1DM, Crohn's, MS or RA. Among women with T1DM, Crohn's or MS, rate of failure to progress was significantly higher than among women without autoimmune disease. Among women with SLE, non-reassuring fetal heart rate

tracing was the most common indication and was nearly three-fold higher than among women without autoimmune disease. Compared to women without autoimmune disease, women with T1DM, SLE, Crohn's or RA had three-to five-fold higher rates of hypertensive disorders as indication for intrapartum cesarean delivery. Women with T1DM had the greatest number of significantly higher rates of indications, including prior uterine scar (90.7/1000), fetal distress (78.9/1000) and elective (47.3/1000).

For indicated preterm deliveries (Table 5), rates of preeclampsia, superimposed preeclampsia, and maternal conditions were higher among women with T1DM, SLE, Crohn's or MS compared to women without autoimmune disease. Women with T1DM had significantly higher rates for nine indications, including chronic hypertension (15.77/1000), fetal anomaly (27.6/1000), fetal macrosomia (1.97/1000), and history of previous pregnancy condition (27.61/1000). Women with SLE had statistically significant higher rates for six indications, including chorioamnionitis (4.95/1000), fetal anomaly (24.75/1000), and other fetal conditions (14.8/1000).

4. Discussion

Despite advances in management of autoimmune disease that aid women in fulfilling family plans, pregnant women with autoimmune diseases continue to experience increased risk of poor obstetric and neonatal outcomes. We found the risk for cesarean delivery after spontaneous or induced labor was similar among women with T1DM. However, the increased risk of overall cesarean delivery for women with SLE, Crohn's, MS or RA may have been due to increased risk of cesarean delivery after spontaneous labor. The increased risk of preterm delivery may be driven by indicated preterm deliveries among women with T1DM or SLE, but both indicated and spontaneous preterm delivery risk were elevated for women with Crohn's, MS or RA.

The richness of the CSL data allowed us to examine indications for cesarean delivery and preterm delivery. Despite heterogeneity of symptoms across types of autoimmune disease, failure to progress, nonreassuring fetal heart rate tracing, and maternal hypertensive disorders were common indications for intrapartum cesarean section across types of autoimmune disease, with evidence particularly strong among women with T1DM (Table 4). Preeclampsia and maternal comorbidities were more likely to be indicators for preterm delivery among women with autoimmune diseases compared to women without autoimmune disease (Table 5). Examining these indications can provide clinicians with new information on risk factors for poor obstetric outcomes among women with autoimmune disease.

These observations among women with a heterogenous set of autoimmune diseases underscores the importance of immunologic health during pregnancy, and the importance of a mother's immunologic health for her neonate. For instance, women with T1DM or SLE had similarly increased risk for a range of adverse obstetric and neonatal outcomes, despite heterogenous symptoms and different target tissues. The observations among women with T1DM or SLE align with previous evidence regarding cesarean delivery, preterm delivery, and small for gestational age births [12,14,17,18,32,41,44–48,57]. We provide the first

evidence among a U.S. cohort that infants born to women with T1DM or SLE were at increased risk for RDS and NICU admission.

Obstetric risks for women with MS or RA have been underexamined in extant literature. Our observation of increased preterm delivery risk among women with MS suggests this association merits further attention. We also add evidence suggesting an increased risk of SGA births among women with RA.

The results which were not statistically significant still provide interesting details regarding obstetric and neonatal risks among women with autoimmune disease. For example, the risk estimates for cesarean delivery after spontaneous labor suggest increased risk among women with SLE, Crohn's, MS or RA, but with a lack of statistical power. Similarly, results suggest infants of women with Crohn's may be at increased risk for SGA and RDS, and women with RA may be at increased risk for cesarean delivery overall and after spontaneous labor, at increased risk for overall and indicated preterm delivery, and RDS, although estimates were imprecise. Additionally, the differences in magnitude of effects observed across autoimmune diseases and obstetric outcomes are notable. For example, the risk for cesarean delivery after induced labor among women with SLE, Crohn's, MS or RA is close to null. These results differ from the 250% increased risk for cesarean delivery after induced labor among women with T1DM, suggesting the risk of poor outcomes is not uniform across autoimmune diseases.

This study has several notable strengths. This is the first study of a large, U.S.-based cohort of pregnant women with a heterogeneous group of autoimmune diseases that assessed multiple obstetric and neonatal outcomes. While the CSL is not a nationally representative sample, the CSL is geographically varied, racially/ethnically diverse and includes women across the reproductive age range, it is a good representation of the pregnancy outcomes among women with autoimmune diseases in the U.S. To the best of our knowledge, this is the first study to examine a large, U.S.-based cohort in which women with T1DM are compared to general population controls. Additionally, we provide the first evidence of NICU admission risk among the infants of women with a variety of autoimmune diseases. We also provide novel evidence that infants born to women with SLE and T1DM are at increased risk for RDS. The neonatal risks observed are not only important in the short-term, but also can impact the health of these children as they age [70,71]. Cohort studies enriched with children born to mothers with autoimmune disease may be required to fully explore these risks due to the rarity of autoimmunity in pregnancy.

Our novel observations fill existing knowledge gaps that can inform clinicians counseling women with autoimmune disease regarding their family plans. There are few resources for clinicians that evaluate common autoimmune disorders and identify the obstetric and neonatal risks for women who are affected. This information allows women with autoimmune disease to make better informed decisions regarding their reproductive health in consultation with their physicians.

The retrospective cross-sectional design of the CSL limited our ability to consider two important aspects of autoimmune disease. First, we do not have data on diagnosis date to

determine the length of time with disease prior to pregnancy. Evidence suggests women who have had an autoimmune disease for a longer period of time have worse health outcomes compared to women who have had the same autoimmune disease for a shorter period of time [72]. Secondly, we do not have data regarding disease management and symptomology during pregnancy. As autoimmune diseases are often managed on a daily basis, the disease activity during pregnancy is known to be an important determinant of pregnancy outcomes. Additionally, CSL data lacks medication use and biologic measures that would be helpful to assess mechanisms linking autoimmune disease and pregnancy outcomes.

Potential mechanisms linking maternal autoimmune disease with obstetric and neonatal outcomes are not well understood. Longitudinal investigations of immunologic health of pregnant women with autoimmune diseases are needed to better understand the general physiology of autoimmune disease during pregnancy, and to understand how daily management of these diseases, including disease flare ups, impacts pregnancy. While advances in the treatment and management of autoimmune disease have aided women in fulfilling their family plans, our data indicate that women with autoimmune disease may still have high risk for adverse outcomes.

Relying on the ICD-9 codes for autoimmune diagnoses may have missed several cases, but we expect that these conditions would be recorded in the medical records since they are likely to cause complications of pregnancy and are relevant for labor and delivery. Since the delivery admission hospitalization record has limited data on maternal chronic disease, we assume the reported risks of poor obstetric and neonatal outcomes among women with autoimmune disease are average risks. We recognize that unmeasured factors such as disease severity, length of time with disease, and management of disease may result in a risk profile differing from our observations. Clinical researchers can build upon this foundation to better understand how risk profiles may differ in order to provide better treatment options and allow for more informed decision making among their patients.

While we did not have treatment or disease severity data, recent recommendations suggest women with autoimmune disease wishing to become pregnant should discuss treatment options with their clinicians [73–79]. Preconception management may include altering medication, as certain treatments for RA, Crohn's and SLE are contraindicated with pregnancy [74,75,77,78]. Management of preconception blood glucose levels may limit risk of nephropathy among women with T1DM, and nephropathy has been suggested as a potential mechanism for increased risk of preeclampsia among women with T1DM [73], and poor glucose control during pregnancy and labor may increase risk for perinatal mortality [80]. During pregnancy, standard course of care is typically recognized as safe for mother and fetus, unless medications have been contraindicated for pregnancy [73–79]. Infants born to women with autoimmune disease may require initial NICU admission or additional examinations per hospital policy, thus clinicians and pregnant women with autoimmune disease should discuss potential care plans covering the immediate postpartum period. For example, women with T1DM should be aware that NICU admission, blood glucose testing, blood lipids testing, and echocardiograms may be included as standard course of care for their infants [79]. Furthermore, clinicians should closely monitor blood glucose levels of women with T1DM during labor and delivery, and insulin drip during labor has been

recommended to maintain blood glucose levels [80]. These findings of increased risk of NICU admission and RDS among neonates suggest more attention to neonates of mothers with autoimmune disease is warranted.

In conclusion, in this comprehensive examination of multiple autoimmune diseases and various obstetric and neonatal outcomes in a national sample of U.S. women and their infants, maternal autoimmune disease was associated with poor obstetric and infant outcomes, especially preterm birth. These increased risks were observed despite the heterogeneity of symptomology across various autoimmune diseases, highlighting the importance of research to better understand immunologic function during pregnancy and to better guide prenatal care and inform patient-provider decision making regarding pregnancy for women with autoimmune disease.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Source of funding

This research was supported by the Intramural Research Program of the National Institutes of Health, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), including funding for the Consortium on Safe Labor (Contract No. HHSN267200603425C) and the Air Quality and Reproductive Health Study (Contract No. HHSN275200800002I, Task Order No. HHSN27500008). This paper has been cleared for publication by the NICHD but the funding source had no role in the design, analysis, interpretation or writing of the manuscript.

References

- [1]. Hayter SM, Cook MC, Updated assessment of the prevalence, spectrum and case definition of autoimmune disease, *Autoimmun. Rev.* 11 (2012) 754–765. [PubMed: 22387972]
- [2]. Lerner A, Jeremias P, Matthias T, The world incidence and prevalence of autoimmune diseases is increasing, *Int. J. Celiac Dis.* 3 (2015) 151–155.
- [3]. Jacobson DL, Gange SJ, Rose NR, Graham NM, Epidemiology and estimated population burden of selected autoimmune diseases in the United States, *Clin. Immunol. Immunopathol.* 84 (1997) 223–243. [PubMed: 9281381]
- [4]. Cooper GS, Stroehla BC, The epidemiology of autoimmune diseases, *Autoimmun. Rev.* 2 (2003) 119–125. [PubMed: 12848952]
- [5]. Mor G, Cardenas I, Abrahams V, Guller S, Inflammation and pregnancy: the role of the immune system at the implantation site, *Ann. N. Y. Acad. Sci.* 1221 (2011) 80–87. [PubMed: 21401634]
- [6]. Challis JR, Lockwood CJ, Myatt L, Norman JE, Strauss JF, Petraglia F, Inflammation and pregnancy, *Reprod. Sci.* 16 (2009) 206–215. [PubMed: 19208789]
- [7]. Mackay IR, Gershwin ME, The nature of autoimmune disease, *Semin. Liver Dis.* 17 (1997) 3–11. [PubMed: 9089906]
- [8]. Mendola P, Laughon SK, Männistö TI, Leishear K, Reddy UM, Chen Z, et al., Obstetric complications among US women with asthma, *Am. J. Obstet. Gynecol.* 208 (2013) 127 e1-e8. [PubMed: 23159695]
- [9]. Mendola P, Männistö TI, Leishear K, Reddy UM, Chen Z, Laughon SK, Neonatal health of infants born to mothers with asthma, *J. Allergy Clin. Immunol.* 133 (2014), <https://doi.org/10.1016/j.jaci.2013.06.012>.

- [10]. Männistö T, Mendola P, Grewal J, Xie Y, Chen Z, Laughon SK, Thyroid diseases and adverse pregnancy outcomes in a contemporary US cohort, *J. Clin. Endocrinol. Metab.* 98 (2013) 2725–2733. [PubMed: 23744409]
- [11]. Persson M, Pasupathy D, Hanson U, Norman M, Birth size distribution in 3,705 infants born to mothers with type 1 diabetes: a population-based study, *Diabetes Care* 34 (2011) 1145–1149. [PubMed: 21430084]
- [12]. Lepercq J, Coste J, Theau A, Dubois-Laforgue D, Timsit J, Factors associated with preterm delivery in women with type 1 diabetes, *A cohort study* 27 (2004) 2824–2828.
- [13]. Cundy T, Slee F, Gamble G, Neale L, Hypertensive disorders of pregnancy in women with Type 1 and Type 2 diabetes, *Diabet. Med. : a journal of the British Diabetic Association* 19 (2002) 482–489.
- [14]. Hanson UI, Persson B, Outcome of pregnancies complicated by type 1 insulin-dependent diabetes in Sweden: acute pregnancy complications, neonatal mortality and morbidity, *Am. J. Perinatol.* 10 (1993) 330–333. [PubMed: 8397576]
- [15]. Kim H-S, Jang H-J, Park J-E, Kim M-Y, Ko S-Y, Kim S-H, Maternal and neonatal outcomes in Korean women with type 1 and type 2 diabetes, *Diabetes & Metabolism Journal* 39 (2015) 316–320. [PubMed: 26301193]
- [16]. Barnabe C, Faris PD, Quan H, Canadian pregnancy outcomes in rheumatoid arthritis and systemic lupus erythematosus, *International Journal of Rheumatology* 2011 (2011) 345727. [PubMed: 22028718]
- [17]. Bundhun PK, Soogund MZ, Huang F, Impact of systemic lupus erythematosus on maternal and fetal outcomes following pregnancy: a meta-analysis of studies published between years 2001–2016, *J. Autoimmun.* 79 (2017) 17–27. [PubMed: 28256367]
- [18]. Barbhaiya M, Bermas BL, Evaluation and management of systemic lupus erythematosus and rheumatoid arthritis during pregnancy, *Clin. Immunol.* 149 (2013) 225–235. [PubMed: 23773975]
- [19]. Phansenee S, Sekararithi R, Jatavan P, Tongsong T, Pregnancy outcomes among women with systemic lupus erythematosus: a retrospective cohort study from Thailand, *Lupus* (2017) 961203317721353.
- [20]. Simard JF, Arkema EV, Nguyen C, Svenungsson E, Wikstrom AK, Palmsten K, et al., Early-onset preeclampsia in lupus pregnancy, *Paediatr. Perinat. Epidemiol.* 31 (2017) 29–36. [PubMed: 27943386]
- [21]. Bharti B, Lee SJ, Lindsay SP, Wingard DL, Jones KL, Lemus H, et al., Disease severity and pregnancy outcomes in women with rheumatoid arthritis: results from the organization of teratology information specialists autoimmune diseases in pregnancy project, *J. Rheumatol.* 42 (2015) 1376–1382. [PubMed: 25877497]
- [22]. Wallenius M, Salvesen KÅ, Daltveit AK, Skomsvoll JF, Rheumatoid arthritis and outcomes in first and subsequent births based on data from a national birth registry, *Acta Obstet. Gynecol. Scand.* 93 (2014) 302–307. [PubMed: 24359405]
- [23]. Spinillo A, Beneventi F, Locatelli E, Ramoni V, Caporali R, Alpini C, et al., The impact of unrecognized autoimmune rheumatic diseases on the incidence of preeclampsia and fetal growth restriction: a longitudinal cohort study, *BMC Pregnancy Childbirth* 16 (2016) 313. [PubMed: 27756248]
- [24]. Konecna B, Laukova L, Vlkova B, Immune activation by nucleic acids: a role in pregnancy complications, *Scand. J. Immunol.* 87 (2018) e12651.
- [25]. Yalcin Serenat E, Yalcin Y, Yavuz A, Akkurt Mehmet O, Sezik M, Maternal and perinatal outcomes in pregnancies with multiple sclerosis: a case-control study, *J. Perinat. Med.* (2017) 455. [PubMed: 27124670]
- [26]. van der Kop ML, Pearce MS, Dahlgren L, Synnes A, Sadovnick D, Sayao A-L, et al., Neonatal and delivery outcomes in women with multiple sclerosis, *Ann. Neurol.* 70 (2011) 41–50. [PubMed: 21710652]
- [27]. Chen YH, Lin HL, Lin HC, Does multiple sclerosis increase risk of adverse pregnancy outcomes? A population-based study, *Multiple Sclerosis Journal* 15 (2009) 606–612. [PubMed: 19318510]

- [28]. Dahl J, Myhr K-M, Daltveit AK, Hoff JM, Gilhus NE, Pregnancy, delivery, and birth outcome in women with multiple sclerosis, *Neurology* 65 (2005) 1961–1963. [PubMed: 16380620]
- [29]. Goldacre A, Pakpoor J, Goldacre M, Perinatal characteristics and obstetric complications in mothers with multiple sclerosis: record-linkage study, *Multiple Sclerosis and Related Disorders* 12 (2017) 4–8. [PubMed: 28283105]
- [30]. Mueller BA, Zhang J, Critchlow CW, Birth outcomes and need for hospitalization after delivery among women with multiple sclerosis, *Am. J. Obstet. Gynecol.* 186 (2002) 446–452. [PubMed: 11904605]
- [31]. Nørgaard M, Larsson H, Pedersen L, Granath F, Askling J, Kieler H, et al., Rheumatoid arthritis and birth outcomes: a Danish and Swedish nationwide prevalence study, *J. Intern. Med.* 268 (2010) 329–337. [PubMed: 20456595]
- [32]. Lin H-C, Chen S-F, Lin H-C, Chen Y-H, Increased risk of adverse pregnancy outcomes in women with rheumatoid arthritis: a nationwide population-based study, *Ann. Rheum. Dis.* 69 (2010) 715–717. [PubMed: 19406733]
- [33]. Chen JS, Ford JB, Roberts CL, Simpson JM, March LM, Pregnancy outcomes in women with juvenile idiopathic arthritis: a population-based study, *Rheumatology* 52 (2013) 1119–1125. [PubMed: 23382363]
- [34]. Mohamed MA, Goldman C, El-Dib M, Aly H, Maternal juvenile rheumatoid arthritis may be associated with preterm birth but not poor fetal growth, *J. Perinatol.* 36 (2016) 268–271. [PubMed: 26675002]
- [35]. Gonzalez-Gonzalez NL, Ramirez O, Mozas J, Melchor J, Armas H, Garcia-Hernandez JA, et al., Factors influencing pregnancy outcome in women with type 2 versus type 1 diabetes mellitus, *Acta Obstet. Gynecol. Scand.* 87 (2008) 43–49. [PubMed: 18158626]
- [36]. Murphy HR, Steel SA, Roland JM, Morris D, Ball V, Campbell PJ, et al., Obstetric and perinatal outcomes in pregnancies complicated by Type 1 and Type 2 diabetes: influences of glycaemic control, obesity and social disadvantage, *Diabet. Med. : a journal of the British Diabetic Association* 28 (2011) 1060–1067.
- [37]. Owens LA, Sedar J, Carmody L, Dunne F, Comparing type 1 and type 2 diabetes in pregnancy—similar conditions or is a separate approach required? *BMC Pregnancy Childbirth* 15 (2015) 69. [PubMed: 25885892]
- [38]. Yves J, Valerie V, Katrien VH, Guy M, Birth weight in type 1 diabetic pregnancy, 2010 *Obstetrics and Gynecology International*, 2010, p. 397623. [PubMed: 21234396]
- [39]. Oron G, Yogev Y, Shcolnick S, Hod M, Fraser G, Wiznitzer A, et al., Inflammatory bowel disease: risk factors for adverse pregnancy outcome and the impact of maternal weight gain, *J. Matern. Fetal Neonatal Med.* 25 (2012) 2256–2260. [PubMed: 22524421]
- [40]. Langen ES, Chakravarty EF, Liaquat M, El-Sayed YY, Druzin ML, High rate of preterm birth in pregnancies complicated by rheumatoid arthritis, *Am. J. Perinatol.* 31 (2014) 009–014.
- [41]. Persson M, Norman M, Hanson U. Obstetric and perinatal outcomes in type 1 diabetic pregnancies: a large, population-based study, *Diabetes Care* 32 (2009) 2005–2009. [PubMed: 19675195]
- [42]. Kelly VM, Nelson LM, Chakravarty EF, Obstetric outcomes in women with multiple sclerosis and epilepsy, *Neurology* 73 (2009) 1831–1836. [PubMed: 19923552]
- [43]. Getahun D, Fassett MJ, Longstreth GF, Koebnick C, Langer-Gould AM, Strickland D, et al., Association between maternal inflammatory bowel disease and adverse perinatal outcomes, *J. Perinatol.* 34 (2014) 435–440. [PubMed: 24651735]
- [44]. Evers IM, de Valk HW, Visser GHA, Risk of complications of pregnancy in women with type 1 diabetes: nationwide prospective study in The Netherlands, *BM J Br. Med. J. (Clin. Res. Ed.)* 328 (2004) 915.
- [45]. Hamed HO, Ahmed SR, Alzolibani A, Kamal MM, Mostafa MS, Gamal RM, et al., Does cutaneous lupus erythematosus have more favorable pregnancy outcomes than systemic disease? A two-center study, *Acta Obstet. Gynecol. Scand.* 92 (2013) 934–942. [PubMed: 23621378]
- [46]. Clowse ME, Jamison M, Myers E, James AH, A national study of the complications of lupus in pregnancy, *Am. J. Obstet. Gynecol.* 199 (2008) 127.e1–127.e6. [PubMed: 18456233]

- [47]. Nili F, McLeod L, O'Connell C, Sutton E, McMillan D, Maternal and neonatal outcomes in pregnancies complicated by systemic lupus erythematosus: a population-based study, *J. Obstet. Gynaecol. Can.* 35 (2013) 323–328. [PubMed: 23660039]
- [48]. Wallenius M, Salvesen KA, Daltveit AK, Skomsvoll JF, Systemic lupus erythematosus and outcomes in first and subsequent births based on data from a national birth registry, *Arthritis Care Res.* 66 (2014) 1718–1724.
- [49]. Broms G, Granath F, Linder M, Stephansson O, Elmberg M, Kieler H, Complications from inflammatory bowel disease during pregnancy and delivery, *Clin. Gastroenterol. Hepatol.* 10 (2012) 1246–1252. [PubMed: 22922307]
- [50]. Hatch Q, Champagne BJ, Maykel JA, Davis BR, Johnson EK, Bleier JS, et al., Crohn's disease and pregnancy: the impact of perianal disease on delivery methods and complications, *Dis. Colon Rectum* 57 (2014) 174–178. [PubMed: 24401878]
- [51]. Ilnyckyyi A, Blanchard JF, Rawsthorne P, Bernstein CN, Perianal Crohn's disease and pregnancy: role of the mode of delivery, *Am. J. Gastroenterol.* 94 (1999) 3274–3278. [PubMed: 10566729]
- [52]. Stephansson O, Larsson H, Pedersen L, Kieler H, Granath F, Ludvigsson JF, et al., Crohn's disease is a risk factor for preterm birth, *Clin. Gastroenterol. Hepatol.* 8 (2010) 509–515. [PubMed: 20202483]
- [53]. Skomsvoll JF, Ostensen M, Irgens LM, Baste V, Pregnancy complications and delivery practice in women with connective tissue disease and inflammatory rheumatic disease in Norway, *Acta Obstet. Gynecol. Scand.* 79 (2000) 490–495. [PubMed: 10857874]
- [54]. Atta DS, Girbash EF, Abdelwahab SM, Abdeldayem HM, Tharwat I, Ghonaim R, Maternal cytokines and disease severity influence pregnancy outcomes in women with rheumatoid arthritis, *J. Matern. Fetal Neonatal Med.* 29 (2016) 3358–3363. [PubMed: 26629845]
- [55]. Dahl J, Myhr K-M, Daltveit AK, Gilhus NE, Pregnancy, delivery and birth outcome in different stages of maternal multiple sclerosis, *J. Neurol.* 255 (2008) 623–627. [PubMed: 18283397]
- [56]. Vanya M, Nyari T, Bencsik K, Bartfai G, Pregnancy and perinatal outcomes among women with multiple sclerosis: a retrospective case-controlled study in South Hungary, *J. Matern. Fetal Neonatal Med.* 27 (2014) 577–581. [PubMed: 23865760]
- [57]. Lateef A, Petri M, Managing lupus patients during pregnancy, *Best Pract. Res. Clin. Rheumatol.* 27 (2013) 435–447. [PubMed: 24238698]
- [58]. Broms G, Granath F, Linder M, Stephansson O, Elmberg M, Kieler H, Birth outcomes in women with inflammatory bowel disease: effects of disease activity and drug exposure, *Inflamm. Bowel Dis.* 20 (2014) 1091–1098. [PubMed: 24810137]
- [59]. O'Toole A, Nwanne O, Tomlinson T, Inflammatory bowel disease increases risk of adverse pregnancy outcomes: a meta-analysis, *Dig. Dis. Sci.* 60 (2015) 2750–2761. [PubMed: 26070523]
- [60]. Davutoglu EA, Ozel A, Yilmaz N, Madazli R, Pregnancy Outcome in 162 Women with Rheumatic Diseases: Experience of a University Hospital in Turkey, *Archives of Gynecology and Obstetrics*, 2017.
- [61]. Vargas R, Repke JT, Ural SH, Type 1 diabetes mellitus and pregnancy, *Reviews in obstetrics & gynecology* 3 (2010) 92–100. [PubMed: 21364860]
- [62]. Buyon JP, Systemic lupus erythematosus, in: Klippel JH, Stone JH, Crofford LJ, White PH (Eds.), *Primer on the Rheumatic Diseases*, Springer New York, New York, NY, 2008, pp. 303–338.
- [63]. Baumgart DC, Sandborn WJ, Inflammatory bowel disease: clinical aspects and established and evolving therapies, *The Lancet* 369 (2007) 1641–1657.
- [64]. Hollenbach JA, Oksenberg JR, The immunogenetics of multiple sclerosis: a comprehensive review, *J. Autoimmun.* 64 (2015) 13–25. [PubMed: 26142251]
- [65]. Heidari B, Rheumatoid Arthritis: early diagnosis and treatment outcomes, *Caspian Journal of Internal Medicine* 2 (2011) 161–170. [PubMed: 24024009]
- [66]. Zhang J, Troendle J, Reddy UM, Laughon SK, Branch DW, Burkman R, et al., Contemporary cesarean delivery practice in the United States, *Am. J. Obstet. Gynecol.* 203 (2010) 326 e1–e10. [PubMed: 20708166]

- [67]. Yasmeen S, Romano PS, Schembri ME, Keyzer JM, Gilbert WM, Accuracy of obstetric diagnoses and procedures in hospital discharge data, *Am. J. Obstet. Gynecol.* 194 (2006) 992–1001. [PubMed: 16580288]
- [68]. Goff SL, Pekow PS, Markenson G, Knee A, Chasan-Taber L, Lindenauer PK, Validity of using ICD-9-CM codes to identify selected categories of obstetric complications, procedures and comorbidities, *Paediatr. Perinat. Epidemiol.* 26 (2012) 421–429. [PubMed: 22882786]
- [69]. Rothman KJ, No adjustments are needed for multiple comparisons, *Epidemiology* 1 (1990) 43–46. [PubMed: 2081237]
- [70]. Engle WA, West KW, Hocutt GA, Pallotto EK, Haney B, Keith RJ, et al., Adult outcomes after newborn respiratory failure treated with extracorporeal membrane oxygenation*, *Pediatr. Crit. Care Med.* 18 (2017) 73–79. [PubMed: 27811529]
- [71]. Boylan J, Alderdice FA, McGowan JE, Craig S, Perra O, Jenkins J, Behavioural outcomes at 3 years of age among late preterm infants admitted to neonatal intensive care: a cohort study, *Arch. Dis. Child. Fetal Neonatal Ed.* 99 (2014) F359–F365. [PubMed: 24812103]
- [72]. Amador-Patarroyo MJ, Rodriguez-Rodriguez A, Montoya-Ortiz G, How does age at onset influence the outcome of autoimmune diseases? *Autoimmune Dis.* 2012 (2012) 251730. [PubMed: 22195277]
- [73]. Feldman AZ, Brown FM, Management of type 1 diabetes in pregnancy, *Curr. Diabetes Rep.* 16 (2016) 76.
- [74]. Krause ML, Makol A, Management of rheumatoid arthritis during pregnancy: challenges and solutions, *Open Access Rheumatol. Res. Rev.* 8 (2016) 23–36.
- [75]. Partlett R, Roussou E, The treatment of rheumatoid arthritis during pregnancy, *Rheumatol. Int.* 31 (2011) 445–449. [PubMed: 21120498]
- [76]. Coyle PK, Management of women with multiple sclerosis through pregnancy and after childbirth, *Therapeutic Advances in Neurological Disorders* 9 (2016) 198–210. [PubMed: 27134675]
- [77]. Stanhope TJ, White WM, Moder KG, Smyth A, Garovic VD, Obstetric nephrology: lupus and lupus nephritis in pregnancy, *Clin. J. Am. Soc. Nephrol. : CJASN* 7 (2012) 2089–2099. [PubMed: 22879437]
- [78]. Cimpoca BA, Nedelea F, Furtuna M, Peltecu G, Panaitescu AM, Managing Crohn's disease during pregnancy, *Masdica* 11 (2016) 221–226.
- [79]. N. C. C. f. W. s. a. C. s. H. (UK, Diabetes in Pregnancy: Management of Diabetes and its Complications from Preconception to the Postnatal Period, National Institute for Health and Care Excellence, London, 2015.
- [80]. Feldman AZ, Brown FM, Management of type 1 diabetes in pregnancy, *Curr. Diabetes Rep.* 16 (2016) 76.

Table 1

Demographic characteristics of women without autoimmune disease and rate per 1000^y (and frequency) of autoimmune disease by demographic variables from the Consortium of Safe Labor, 2002–2008 (n = 205521).

	Women without autoimmune disease (N = 204384)	Autoimmune Disease Rate of disease per 1000 (n)				
		Type 1 Diabetes 2.4 (507)	Systemic Lupus Erythematosus 0.9 (202)	Crohn's Disease 0.8 (169)	Multiple Sclerosis 0.7 (146)	Rheumatoid Arthritis 0.5 (123)
Race						
White	514.4 (105136)	2.6 (280)	0.9 (99)	1.4 (144)	1.0 (104)	0.8 (81)
Black	208.3 (42576)	2.9 (124)	1.3 (57)	0.5 (20)	0.7 (28)	0.5 (20)
Hispanic	168.5 (34439)	2.0 (70)	0.9 (30)	<0.1 (1)	0.2 (8)	0.3 (10)
Other	108.7 (22233)	0.1 (33)	<.01 (16)	<0.1 (4)	<0.1 (6)	<0.1 (12)
	<i>p</i> < 0.01	<i>p</i> < 0.01	<i>p</i> = 0.16	<i>p</i> < 0.01	<i>p</i> < 0.01	<i>p</i> = 0.02
Age						
< 20	92.7 (18953)	2.5 (47)	0.3 (6)	0.5 (9)	0.1 (2)	0.6 (12)
20-24	253.6 (51829)	2.4 (127)	0.9 (49)	0.5 (25)	0.3 (15)	0.3 (14)
25-29	280.4 (57304)	2.4 (136)	0.9 (52)	1.0 (56)	0.6 (34)	0.4 (22)
30-34	224.2 (45826)	2.6 (121)	1.4 (64)	1.1 (52)	1.2 (55)	0.8 (36)
>=35	149.1 (30472)	2.5 (76)	1.0 (31)	0.9 (27)	1.3 (40)	1.3 (39)
	<i>p</i> < 0.01	<i>p</i> = 0.70	<i>p</i> < 0.01	<i>p</i> < 0.01	<i>p</i> < 0.01	<i>p</i> < 0.01
Insurance						
Private	571.6 (116823)	2.5 (299)	1.1 (135)	1.1 (127)	0.9 (102)	0.7 (79)
Public	303.3 (61982)	2.9 (181)	1.0 (65)	0.5 (34)	0.5 (32)	0.6 (36)
Other	125.1 (25578)	0.9 (27)	0.1 (2)	0.3 (8)	0.5 (12)	0.3 (8)
	<i>p</i> < 0.01	<i>p</i> < 0.01	<i>p</i> < 0.01	<i>p</i> < 0.01	<i>p</i> = 0.02	<i>p</i> = 0.19
Region						
Northeast	190.6 (38958)	1.7 (67)	0.7 (26)	1.4 (54)	0.8 (32)	0.7 (29)
South	388.1 (79336)	2.9 (228)	1.4 (115)	0.8 (61)	0.7 (55)	0.7 (57)
Midwest	102.3 (20919)	3.1 (65)	0.9 (18)	0.9 (18)	0.7 (15)	0.4 (9)
West	318.8 (65171)	2.2 (147)	0.7 (43)	0.5 (36)	0.7 (44)	1.4 (28)
	<i>p</i> < 0.01	<i>p</i> < 0.01	<i>p</i> < 0.01	<i>p</i> < 0.01	<i>p</i> = 0.84	<i>p</i> = 0.06

p-values assessed using fisher's exact test.

R_{p} Rates per 1000 are specific for each demographic category (rate = (outcome n/ autoimmune disease N)* 1000).

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Rate per 1000^a (and frequency) of obstetric and neonatal outcomes for singleton pregnancies from the Consortium of Safe Labor 2002–2008 (n = 205521).

Table 2

	Women without autoimmune disease (n = 204384)	Autoimmune Disease				
		Type I Diabetes (n = 507)	Systemic Lupus Erythematosus (n = 202)	Crohn's Disease (n = 169)	Multiple Sclerosis (n = 146)	Rheumatoid Arthritis (n = 123)
Cesarean Delivery	278.5 (56926)	670.6 (340) ^b	391.1 (79) ^b	360.9 (61) ^b	424.7 (62) ^b	390.2 (48) ^b
<i>Prelabor cesarean</i>	113.6 (23218)	270.2 (137) ^b	183.2 (37) ^b	183.4 (31) ^b	232.9 (34) ^b	211.4 (26) ^b
<i>After spontaneous labor</i>	93.0 (19016)	195.3 (99) ^b	123.8 (25)	118.3 (20)	123.3 (18)	130.1 (16)
<i>After induced labor</i>	71.9 (14692)	205.1 (104) ^b	84.2 (17)	59.2 (10)	68.5 (10)	48.8 (6)
Preterm Birth	111.0 (22701)	426.0 (216) ^b	376.2 (76) ^b	195.3 (33) ^b	191.7 (28) ^b	178.8 (22) ^b
<i>Spontaneous</i>	78.4 (16038)	248.5 (126) ^b	232.7 (47) ^b	130.1 (22) ^b	143.8 (21) ^b	154.4 (19) ^b
<i>Indicated</i>	17.8 (3650)	145.9 (74) ^b	103.9 (21) ^b	29.5 (5) ^b	27.3 (4)	16.2 (2)
Preeclampsia	46.4 (9498)	159.7 (81) ^b	138.6 (28) ^b	82.8 (14) ^b	61.6 (9)	81.3 (10)
NICU Admission	115.4 (23593)	408.2 (207) ^b	282.1 (57) ^b	195.3 (33) ^b	164.3 (24)	195.1 (24) ^b
Neonatal Respiratory Distress Syndrome	31.1 (6357)	130.1 (66) ^b	113.8 (23) ^b	47.3 (8)	34.0 (5)	48.7 (6)
Small for Gestational Age	109.3 (22350)	65.0 (33) ^b	178.2 (36) ^b	124.2 (21)	75.3 (11)	170.7 (21) ^b
Perinatal Mortality	5.9 (1214)	13.8 (7) ^b	19.8 (4) ^b	5.9 (1)	0 (0)	0 (0)

^aRates per 1000 are specific for each autoimmune disease category (rate = (outcome n/autoimmune disease N)*1000).

^bp < 0.05 indicates rates among women with autoimmune disease different than rates among women without autoimmune disease. P-values obtain using generalized estimating equations to account for women who had more than one pregnancy in the study.

The association between autoimmune disease and adverse obstetric and neonatal outcomes among women with autoimmune disease and their infants in the Consortium of Safe Labor Singleton Pregnancies (n = 205521), 2002–2008.

Table 3

	Women without autoimmune disease (n = 204384)	Type 1 Diabetes (n = 507) RR (95% CI)	Systemic Lupus Erythematosus (n = 202) RR (95% CI)	Crohn's Disease (n = 169) RR (95% CI)	Multiple Sclerosis (n = 146) RR (95% CI)	Rheumatoid Arthritis (n = 123) RR (95% CI)
Cesarean	Reference	2.16 (2.02, 2.32)*	1.21 (1.02, 1.44)*	1.31 (1.08, 1.60)*	1.33 (1.11, 1.61)*	1.18 (0.94, 1.49)
<i>Prelabor</i>	Reference	1.13 (1.09, 1.16)*	1.03 (0.99, 1.08)	1.05 (1.00, 1.11)*	1.07 (1.02, 1.13)*	1.05 (0.99, 1.11)
<i>After Induction</i>	Reference	2.58 (2.17, 3.06)*	1.05 (0.66, 1.66)	0.91 (0.50, 1.64)	0.96 (0.53, 1.74)	0.64 (0.29, 1.43)
<i>After Spontaneous</i>	Reference	1.90 (1.61, 2.26)*	1.23 (0.86, 1.77)	1.36 (0.90, 2.05)	1.23 (0.80, 1.87)	1.33 (0.85, 2.09)
Preterm	Reference	3.52 (3.17, 3.91)*	2.90 (2.42, 3.48)*	1.84 (1.37, 2.49)*	1.67 (1.20, 2.30)*	1.42 (0.97, 2.07)
<i>Indicated</i>	Reference	7.12 (5.73, 8.84)*	4.59 (3.05, 6.91)*	1.79 (0.76, 4.20)	1.48 (0.57, 3.81)	0.80 (0.20, 3.10)
<i>Spontaneous</i>	Reference	3.06 (2.61, 3.58)*	2.62 (2.01, 3.40)*	1.68 (1.12, 2.53)*	1.73 (1.14, 2.64)*	1.87 (1.23, 2.86)*
Preeclampsia	Reference	1.11 (1.02, 1.20)*	1.09 (0.96, 1.24)	1.03 (0.89, 1.20)	1.02 (0.87, 1.19)	1.03 (0.87, 1.23)
Small for Gestational Age	Reference	0.61 (0.43, 0.86)*	1.68 (1.21, 2.32)*	1.26 (0.82, 1.93)	0.76 (0.42, 1.38)	1.66 (1.08, 2.55)*
Respiratory Distress Syndrome	Reference	3.62 (2.84, 4.62)*	2.99 (1.99, 4.51)*	1.62 (0.81, 3.23)	1.08 (0.45, 2.58)	1.44 (0.65, 3.21)
NICU	Reference	1.25 (1.16, 1.35)*	1.13 (1.00, 1.28)*	1.07 (0.93, 1.23)	1.04 (0.89, 1.21)	1.06 (0.90, 1.25)
Admission						
Perinatal Mortality/rowhead	Reference	2.35 (1.12, 4.91)*	–	–	–	–

Models adjusted for maternal age, maternal race/ethnicity, preconception body mass index, health insurance, marital status, smoking in pregnancy, alcohol use in pregnancy, other chronic diseases, and census region.;

* p < .05 indicates rates among women with autoimmune disease different than rates among women without autoimmune disease.

Table 4

Rate per 1,000^a (and frequency) of intrapartum cesarean delivery: overall and by indication.

	Women without autoimmune disease (n = 204,384)	Type I Diabetes (n = 507)	Systemic Lupus Erythematosus (n = 202)	Crohn's Disease (n = 169)	Multiple Sclerosis (n = 146)	Rheumatoid Arthritis (n = 123)
Intrapartum Cesarean Delivery	164.9 (33708)	400.3 (203) ^c	207.9 (42)	177.5 (30)	191.7 (28)	178.8 (22)
Failure to progress	65.5 (13394)	149.9 (76) ^c	44.5 (9) ^c	88.7 (15) ^c	95.8 (14) ^c	48.7 (6) ^c
NRFHRT ^b	37.7 (7714)	78.9 (40) ^c	113.8 (23) ^c	29.5 (5)	6.8 (1) ^c	40.6 (5)
Prior uterine scar	33.5 (6856)	90.7 (46) ^c	34.6 (7)	11.8 (2) ^c	41.0 (6)	48.7 (6)
Breech	14.9 (3057)	19.7 (10)	4.9 (1)	17.7 (3)	27.3 (4) ^c	8.1 (1)
Elective	11.1 (2273)	47.3 (24) ^c	19.8 (4)	5.9 (1)	0 (0)	8.1 (1)
Other	10.1 (2082)	19.7 (10)	0 (0)	11.8 (2)	20.5 (3)	0 (0)
Hypertensive disorder	3.3 (685)	19.7 (10) ^c	14.8 (3) ^c	11.8 (2) ^c	0 (0)	16.2 (2) ^c
Failed induction	2.6 (551)	9.8 (5) ^c	9.9 (2) ^c	0 (0)	0 (0)	0 (0)
Chorioamnionitis	1.5 (326)	0 (0)	0 (0)	5.9 (1)	0 (0)	0 (0)
Fetal indication	1.9 (404)	3.8 (2)	0 (0)	5.9 (1)	6.8 (1)	0 (0)
Placenta abruptio	0.9 (188)	1.9 (1)	4.9 (1)	5.9 (1)	0 (0)	0 (0)
Placenta previa	0.7 (160)	1.9 (1)	0 (0)	0 (0)	6.8 (1)	0 (0)
Emergency	0.7 (149)	1.9 (1)	4.9 (1)	0 (0)	0 (0)	8.1 (1)
HIV/Herpes	0.6 (137)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Failed forceps/vacuum	0.5 (110)	1.9 (1)	0 (0)	0 (0)	0 (0)	0 (0)
Failed VBAC	0.2 (46)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Shoulder dystocia	0.07 (15)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
History of shoulder dystocia	0.06 (14)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

^aCategories for the indicated precursors are not mutually exclusive as multiple obstetric or fetal conditions were included in the same pregnancy.

^bNRFHRT, non-reassuring fetal heart rate tracing.

^cp < 0.05 Indicates rate among women with autoimmune disease different than rate among women without autoimmune disease.

Table 5

Rate per 1,000^a (and frequency) of indicated PTB: overall and by indication.

	Women without autoimmune disease (n = 204,384)	Type I Diabetes (n = 507)	Systemic Lupus Erythematosus (n = 202)	Crohn's Disease (n = 169)	Multiple Sclerosis (n = 146)	Rheumatoid Arthritis (n = 123)
Indicated Preterm Delivery	17.8 (3650)	145.9 (74) [*]	103.9 (21) [*]	29.5 (5) [*]	27.3 (4)	16.2 (2)
Preeclampsia (all)	6.59 (1348)	47.33 (24) [*]	29.70 (6) [*]	17.75 (3)	6.84 (1)	0 (0)
Maternal Condition ^b	4.95 (1012)	43.39 (22) [*]	49.50 (10) ^b	17.75 (3) [*]	6.84 (1)	0 (0)
Admission for maternal reason	2.98 (611)	27.61 (14) [*]	14.85 (3)	11.83 (2)	0 (0)	0 (0)
History of pregnancy condition ^c	2.89 (592)	27.61 (14) [*]	24.75 (5)	5.91 (1)	6.84 (1)	8.13 (1)
Fetal anomaly	2.64 (540)	27.61 (14) [*]	24.75 (5) [*]	0 (0)	0 (0)	8.13 (1)
Fetal condition ^d	2.16 (443)	7.88 (4)	14.85 (3) [*]	0 (0)	0 (0)	0 (0)
Gestational diabetes	1.89 (388)	0 (0)	4.95 (1)	11.83 (2)	13.69 (2)	8.13 (1)
Superimposed Preeclampsia	1.68 (345)	23.66 (12) [*]	4.95 (1) [*]	5.91 (1)	6.84 (1)	0 (0)
Stillbirth	1.51 (310)	3.94 (2)	4.95 (1)	0 (0)	0 (0)	0 (0)
Pregestational diabetes	1.25 (256)	145.9 (74)	9.90 (2)	5.91 (1)	0 (0)	0 (0)
Gestational Hypertension	1.23 (252)	11.83 (6)	9.90 (2)	0 (0)	0 (0)	0 (0)
Maternal Fever	1.15 (237)	7.88 (4)	4.95 (1)	0 (0)	0 (0)	0 (0)
Admission for fetal reason ^e	1.12 (229)	3.94 (2)	4.95 (1)	0 (0)	0 (0)	0 (0)
Chronic hypertension	0.94 (194)	15.77 (8) [*]	9.90 (2)	0 (0)	0 (0)	8.13 (1)
Abruption	0.81 (167)	1.97 (1)	9.90 (2)	0 (0)	0 (0)	0 (0)
Prior uterine scar	0.67 (138)	1.97 (1)	0 (0)	0 (0)	0 (0)	0 (0)
Unspecified HTN	0.27 (57)	1.97 (1) [*]	0 (0)	0 (0)	6.84 (1)	0 (0)
Chorioamnionitis	0.25 (53)	1.97 (1)	4.95 (1) [*]	0 (0)	0 (0)	0 (0)
Fetal macrosomia	0.20 (42)	1.97 (1) [*]	0 (0)	0 (0)	0 (0)	0 (0)
Vaginal bleeding	0.20 (41)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Previa	0.13 (28)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Eclampsia	0.12 (26)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

^{*} *p* < 0.05 Indicates rate among women with autoimmune disease different than rate among women without autoimmune disease.

^gCategories for the indicated precursors are not mutually exclusive as multiple obstetric or fetal conditions were included in the same pregnancy.

^hMaternal conditions included maternal medical problems such as cardiac or renal disease.

^cHistory of maternal or fetal condition included pregnancy complications in a previous pregnancy only.

^dFetal conditions included intrauterine growth restriction and abnormal antenatal testing.

^eAdmission for fetal or maternal reason was included only if there was no other pregnancy condition.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript