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The Importance of Pregnancy Planning in Lupus Pregnancies

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Abstract

Objective: In seeking new approaches to improve lupus pregnancy outcomes, we study the association between pregnancy planning, behaviors recommended by American College of Rheumatology's Reproductive Health Guideline 2020, and pregnancy and infant outcomes.

Methods: Lupus pregnancies in a prospective registry (1/1/2018 to 4/1/2020) were classified as planned or not-planned using the patient-reported London Measure of Unplanned Pregnancy. These groups were compared for demographics, pre-pregnancy disease activity, pregnancy planning behaviors, and delivery outcomes.

Results: Among 43 women with 43 singleton pregnancies the average age was 29.4 years and 42% were Black. Overall, 60% were planned pregnancies and 40% were not-planned (16 ambivalent, 1 unplanned). Women with not-planned pregnancies had lower age, income, and education, and more required Medicaid. Women with not-planned pregnancies were more likely to conceive when lupus activity was higher (p=0.001), less likely to receive pre-pregnancy counseling with a rheumatologist (p=0.02), and less likely to continue pregnancy-compatible medications (p=0.03). Severe PROMISSE adverse pregnancy outcomes (APOs) and severe neonatal outcomes were higher among women with not-planned than planned pregnancies (43% vs 0% p=0.003; 70% vs 30% p=0.06).

Conclusion: This study identifies pregnancy intention as a potentially modifiable risk factor for poor outcomes in women with lupus. It highlights a unique population of women with lupus at high risk for pregnancy and infant complications: those ambivalent about pregnancy. These women may not be effectively engaging in health behaviors that prevent pregnancy nor those that

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will prepare for a safe pregnancy. With effective pregnancy planning and contraception guidance, we may decrease their risk for maternal-fetal morbidity and mortality.

Keywords

Pregnancy; Systemic Lupus Erythematosus; Antiphospholipid Syndrome

INTRODUCTION:

Pregnancies in women with systemic lupus erythematosus (lupus) are at higher risk for adverse outcomes as compared to the general population. Studies have shown that up to 20% of lupus pregnancies result in pregnancy loss, up to 40% deliver preterm, and up to 15% are diagnosed with preeclampsia.[1-3] Research advances in the field of reproductive rheumatology as well as the recently published American College of Rheumatology's Reproductive Health Guideline (ACR 2020) have helped standardize the clinical management of lupus pregnancies.[4] The ACR 2020 Guideline recommend that women with lupus conceive when disease activity has been clinically mild or quiescent in the 6 months prior to pregnancy to decrease the risk of adverse outcomes. Furthermore, women are recommended to continue on pregnancy-compatible lupus medications through pregnancy to manage lupus activity and reduce the risk of flares.

Clinical management of lupus pregnancies begins in the pre-pregnancy period and requires active patient engagement. The role of patient pregnancy planning and pregnancy intention, however, has not been well-studied in women with lupus. We hypothesize that women with lupus who have planned pregnancies will be more likely to engage in ACR guideline-recommended pregnancy behaviors as compared to women who are ambivalent about pregnancy or those who have unplanned pregnancies. We additionally hypothesize that women with planned pregnancies will have better delivery outcomes and fewer pregnancy complications. Data from a prospective pregnancy registry were used to analyze differences in outcomes between planned and not-planned pregnancies.

MATERIALS AND METHODS:

The Maternal Autoimmune Disease Research Alliance (MADRA) Registry was approved by the Duke University Institutional Review Board as a prospective pregnancy registry (Pro00084014; 1/1/2018 to 4/1/2020). Informed consent for registry enrollment was obtained during the first rheumatology clinic visit in pregnancy. Patients in the registry received standard-of-care visits through pregnancy and completed their study involvement with a single postpartum visit. Diagnosis with lupus was either confirmed or established using the Systemic Lupus Collaborating Clinics (SLICC) criteria. Demographics were obtained at the initial visit along with information on pregnancy intention using the London Measure of Unplanned Pregnancy (LMUP) survey.[5, 6] A Physician Global Assessment (PGA) Score (score 0-3) was documented at each visit, serving as a physician-reported measure of lupus disease activity during pregnancy (MEBC). Delivery outcomes were obtained through both chart review and patient report at the postpartum visit. Additional data

on comorbidities, medication use, hospitalizations, and neonatal outcomes were obtained through retrospective chart review (AR).

LMUP:

At the initial visit, patients filled out the validated London Measure of Unplanned Pregnancy Survey (LMUP).[5-8] The LMUP consists of 6 questions to assess the degree to which the current pregnancy was planned, specifically with regards to contraception use, pregnancy timing, pregnancy intention, pregnancy desire, partner agreement, and pregnancy planning behaviors. The responses to each of these 6 questions receive a score of 0 (response that denotes unplanned), 1 (ambivalent), or 2 (planned) for a maximum LMUP total score of 12. Pregnancies are classified based on the LMUP total score as planned (score 10-12), ambivalent (score 4-9), or unplanned (score 0-3). In this study, pregnancies in the ambivalent and unplanned groups were combined to create a not-planned group (score 0-9) versus a planned group (score 10-12).

Individual LMUP questions were analyzed for the entire cohort and with regards to pregnancy planning. The LMUP survey included questions regarding pregnancy planning behaviors such as seeking medical / health advice, taking prenatal vitamins or folic acid, stopping or cutting down on alcohol, stopping or cutting down on smoking, eating more healthily, or other actions such as exercise or weight-loss. Women were additionally asked if they changed medications for rheumatic disease in our version of the LMUP survey.

Pre-pregnancy Lupus Activity:

Patient charts in the one year prior to pregnancy were deidentified (AR), reviewed (MEBC), and retrospectively assigned a PGA Score (score 0-3; a score of 0 indicates no lupus activity while a score of 3 indicates highly active disease) (MEBC) to characterize lupus activity in the 6 months prior to conception.

Delivery Outcomes:

Live births were considered term if delivery occurred ≥ 37 weeks of gestation and preterm if delivery occurred < 37 weeks of gestation. A pregnancy loss was considered a stillbirth if it occurred ≥ 20 weeks and a miscarriage if it occurred < 20 weeks. Preeclampsia was diagnosed at ≥ 20 weeks according to the clinical judgement of the treating obstetrician. Small for gestational age was calculated at the 5^{th} and 10^{th} birthweight percentiles using birthweight, sex, and gestational age at delivery.[9] Composite variables from the PROMISSE study were used to measure adverse pregnancy outcomes (APOs).[10] PROMISSE APO criteria include neonatal death, fetal death > 12 weeks, preeclampsia, preterm delivery < 36 weeks, or small for gestational age (SGA) < 5th percentile. Severe PROMISSE-APO criteria include neonatal death, fetal death > 12 weeks, preeclampsia and preterm delivery < 34 weeks, or preterm delivery < 30 weeks. Pregnancy losses < 12 weeks were excluded in APO analysis as in the PROMISSE study. Among live births, a composite variable was developed for severe neonatal outcomes and included neonatal death, neonatal intensive care unit (NICU) stay > 1 week, APGAR < 7 at 5 minutes, or SGA < 5th percentile.

Medication Use:

Data on rheumatic medication usage in the pre-pregnancy period and during pregnancy was obtained through retrospective chart review (AR). Hydroxychloroquine serum drug levels at the initial visit were obtained either clinically through the Mayo Clinic lab and accessed through chart review or through research blood samples that were collected and processed retrospectively. Hydroxychloroquine serum levels were characterized as low (≤ 100 ng/mL) or normal (> 100 ng/mL) (SJB).[11] Levels were not obtained for patients reporting not taking the medication (n=4), patients that did not consent to donating research blood (n=4), or patients unable to have a blood draw on the day of their visit due to logistical constraints (n=7).

Statistical Analysis:

Categorical outcomes were compared between planned and not-planned pregnancies using Fisher's Exact tests, and continuous variables were compared using t-tests for independent samples and Wilcoxon rank-sum tests for means and medians, respectively. Composite delivery outcomes were additionally analyzed by demographics and pre-pregnancy lupus activity.

Analysis was performed using SAS 9.4 (Cary, North Carolina). Study data was collected and managed using REDCap electronic data capture tools hosted at Duke University.[12,13] All protected health information was stored behind a Duke University firewall (electronically) or in a locked cabinet (printed documents).

RESULTS:

This study included 43 singleton lupus pregnancies in 43 women; 3 pregnancies were excluded due to missing LMUP data.

Demographics and Comorbidities:

In this cohort, the average maternal age at delivery was 29.4 ± 5.4 years with 42% of the cohort identifying as Black and 9% (n=4) identifying as Hispanic. Women with not-planned pregnancies were more likely to be young, single, have less than a college education, have an annual income less than $50,000, and need Medicaid during pregnancy as opposed to having private health insurance (Table 1). A total of 10 women had documented chronic hypertension and the prevalence of hypertension was similar between not-planned and planned pregnancies. None of the women in this cohort were diagnosed with diabetes mellitus. Three women in this cohort had documented anti-phospholipid syndrome which was managed with aspirin and enoxaparin during pregnancy and the postpartum period.

Pre-pregnancy Lupus Activity:

In this cohort, the average PGA at the time of conception was 0.6 ± 0.6. Disease activity in the 6 months prior to conception was significantly higher in not-planned pregnancies than planned pregnancies (1.0 ± 0.6 vs. 0.3 ± 0.5; p=0.001). Of note, 3 women in this cohort had active nephritis, all of whom had not-planned pregnancies; 2 women had severe cutaneous lesions, one of whom had a not-planned pregnancy.

LMUP Survey:

Overall, 26 women had planned pregnancies (60%) and 17 women had not-planned pregnancies (40%) (Table 2). Of the not-planned pregnancies (n=17), only one woman had a truly unplanned pregnancy which was the result of contraception failure on oral contraceptives, while the rest were ambivalent regarding pregnancy (n=16). Pregnancy ambivalence refers to some engagement with planning-related intentions and behaviors but not enough to be considered a planned pregnancy as per the LMUP scoring system. Women with planned pregnancies were significantly more likely than those with not-planned pregnancies to feel pregnancy happened at the right time (88% vs. 12%; $p<0.0001$), intend pregnancy (85% vs. 12%; $p<0.0001$), desire a baby (96% vs. 24%; $p<0.0001$), and agree on pregnancy with their partner (100% vs. 24%; $p<0.0001$). None of the patients with planned pregnancies were using contraception in the month that they became pregnant consistent with expected behavior prior to a planned pregnancy. Among women with not-planned pregnancies, 76% used no contraception in the month prior to conception, 24% used contraception “sometimes” or had known contraception failures, and none reported using contraception all of the time.

While 69% of women with planned pregnancies engaged in two or more planning behaviors, only 12% of not-planned pregnancies engaged in two or more behaviors ($p=0.0004$) (Table 3). Likewise, 8% of planned pregnancies engaged in no planning behaviors while 71% of not-planned pregnancies engaged in no planning behaviors. While 77% of women with planned pregnancies were taking prenatal vitamins or folic acid prior to pregnancy, only one woman with a not-planned pregnancy reported doing the same. The rate of pre-pregnancy counseling was higher among planned pregnancies with 58% receiving some form of pre-pregnancy counseling with a rheumatologist prior to pregnancy as compared to the 19% of women with not-planned pregnancies ($p=0.02$).

Delivery Outcomes:

Delivery outcomes were missing for 8 pregnancies as patients had either not delivered as of 4/1/2020 (n=7) or data was unavailable through chart review (n=1). Of the 35 pregnancies with available outcomes, 20 (57%) were planned and 15 (43%) were not-planned (14 ambivalent, 1 unplanned). Overall, 83% of the pregnancies resulted in a live birth, of which 34% were preterm deliveries (Supplemental Table 1). The average gestational age at live delivery for the cohort was 36.2 ± 3.4 weeks, 24% of infants were SGA < 10th percentile, and 27% of pregnancies were complicated by preeclampsia. Of the pregnancies that resulted in non-live births, there were 4 miscarriages, 1 stillbirth at 21 weeks, and 1 medically indicated termination of a wanted pregnancy at 8 weeks for moderate-severe pulmonary hypertension.

Overall, the rate of PROMISSE-APO was 61% and Severe PROMISSE-APO was 18% (Table 4). Among live births, the rate of a severe neonatal outcome was 45%. Not-planned pregnancies had a higher rate of Severe PROMISSE-APOs as compared to planned pregnancies (43% vs. 0%; $p=0.003$) and a higher rate of severe neonatal outcomes (70% vs. 32%; $p=0.06$). Analysis of delivery outcomes by pre-pregnancy lupus activity revealed that patients with PGA ≥ 1.5 were more likely to have a Severe PROMISSE-APO (60% vs. 11%;

p=0.03) and severe neonatal outcome (100% vs. 36%; p=0.03). Multivariate analysis could not be performed due to the limited sample size; however, even among women with lower lupus activity (PGA < 1.5), not-planned pregnancies had higher rates of complications. Compared to planned pregnancies in women with low lupus activity, not-planned pregnancies with high lupus activity were more likely to result in a Severe PROMISSE-APO (30% vs. 0%; p=0.04), PROMISSE-APO (70% vs. 50%; p=0.3), and severe neonatal outcome (57% vs. 28%; p=0.2). There were no significant differences in delivery outcomes by demographics including race, age, education, marital status, health insurance status, or income (Supplemental Table 2).

Disease Activity and Hospital Visits:

In this cohort, the average maximum PGA during pregnancy was 0.8 ± 0.7. Women with not-planned pregnancies had more lupus activity during pregnancy as compared to women with planned pregnancies (PGA 1.1 ± 0.8 vs. 0.6 ± 0.7; p=0.05) (Table 5). Overall, 40% of women required an average daily dose of prednisone > 7.5 mg through pregnancy, including 60% of women with not-planned pregnancies.

In this cohort, 19 women (54%) had a documented 40 hospital visits (Emergency Department, obstetric triage unit, or admission to the hospital) during pregnancy for any reason outside of delivery. Specifically, 7 women had a documented 11 lupus-related hospital visit, including 33% of not-planned pregnancies and 10% of planned pregnancies (p=0.1). Reasons for lupus-related hospital visits included CNS lupus, lupus nephritis, pericarditis, serositis, hemolytic anemia, pancytopenia, and worsening pulmonary hypertension. A higher number of women with not-planned pregnancies required a hospital visit for any reason during pregnancy (80% vs. 35%; p=0.02). The mean number of hospital visits and the median length of stay in the hospital were not different between groups. Reasons for non-lupus-related hospital visits included chronic hypertension, asthma, infections, musculoskeletal chest pain, fetal heart block, preeclampsia rule-out, preterm labor rule-out, vaginal bleeding, and symptoms such as edema, nausea, vomiting, and abdominal cramping.

Medications:

Continuing pregnancy-compatible medications through conception and pregnancy is an important recommendation within the ACR Reproductive Health Guideline to keep lupus activity quiescent. In this cohort, 46% of women with not-planned and 16% of women with planned pregnancies (p=0.06) discontinued at least one pregnancy-compatible lupus medication in the periconception period (Table 6). Among not-planned pregnancies, hydroxychloroquine (4/13, 31%) and azathioprine (2/3, 67%) were the most frequently discontinued. Among planned pregnancies, azathioprine (2/9, 22%) was the most often discontinued medication. All of the women with not-planned pregnancies and 30% of women with planned pregnancies (p<0.0001) received a prescription to either start or re-start a pregnancy-compatible lupus medication.

Hydroxychloroquine levels were measured on a subset of patients and demonstrated that half of the patients with both planned and not-planned pregnancies with serum drug levels were

non-adherent to the drug. However, numerically more patients who received pre-pregnancy counseling were found to be adherent to hydroxychloroquine as compared to patients who did not receive counseling (75% vs. 36%; p=0.2).

In this cohort, 7 women (16%) conceived on a pregnancy-incompatible medication including an ACE-inhibitor/ARB (n=4), mycophenolate (n=3), and belimumab (n=2). None of the women in this cohort conceived on cyclophosphamide, leflunomide, methotrexate, rituximab, or pregnancy-incompatible anticoagulants. There were no differences between planned and not-planned pregnancies in this regard. None of these women had a pregnancy loss, and per chart review, there were no documented birth defects in the delivery record from any of these exposures. All those who conceived on a pregnancy-incompatible medication discontinued it in early pregnancy.

DISCUSSION:

In this study, almost all of the not-planned pregnancies were in women who were ambivalent about pregnancy as opposed to having a truly unplanned pregnancy. Women with lupus who had not-planned pregnancies had significantly more complicated pregnancies with higher rates of severe infant complications as compared to women who had planned pregnancies. Furthermore, pregnancies in women who were not-planned were less likely to be conceived and managed according to ACR Reproductive Health Guideline. Specifically, these pregnancies were less likely to receive pre-pregnancy counseling with a rheumatologist, conceive when lupus activity was well-controlled, and continue pregnancy-compatible lupus medications. Moreover, most of them required a hospital visit outside of delivery, almost half of their pregnancies resulted in a severe pregnancy outcome, and the majority of the infants experienced a severe outcome. While prior research has focused on identifying biologic predictors of pregnancy complications in women with lupus, this work suggests that identifying women who are at-risk based on their pregnancy intent – with specific attention to women who are neither committed to getting pregnant nor to actively avoiding conception – may be a new opportunity to change the trajectory of lupus pregnancy outcomes.

Conception when a pregnancy is not planned is a common occurrence world-wide and among all populations. In cohort studies of women in European countries, anywhere from 44-83% of pregnancies were planned, and in an LMUP validation study by Morof et al., American women reported a lower planned pregnancy prevalence of 30%.[7, 14-20] Overall, the rate of planned pregnancies in this study (60%) was consistent with that seen in other Western nations and twice that reported among American women.[7] Furthermore, in comparison to a cohort of women with HIV in the United States, in which ambivalence was very common (58%) and only 19% of pregnancies were planned, the women with lupus in this cohort demonstrated much higher rates of planning.[21] Among these populations, the rate of pregnancy ambivalence is higher in women with significant socioeconomic disadvantages. [22-25]

Globally, pregnancy planning can impact the risk for pregnancy loss, low birth weight, and preterm birth. Cohort studies in Ethiopia, India, and Bangladesh have demonstrated that a lack of pregnancy planning is a predictor of pregnancy loss and severe neonatal outcomes in

those populations, but these associations were not seen among population-based studies in the United Kingdom and Belgium.[16, 17, 26-29] However, the association between a lack of pregnancy planning and low birthweight (< 2500 grams) as well as preterm delivery (< 37 weeks) has been demonstrated in several cohort studies of American woman as well as in the larger global population.[30-33] A meta-analysis by Hall et al. suggests that unintended pregnancies have 1.4-times the odds of delivering a low-birth weight baby and 1.3-times the odds of delivering a preterm baby.[34, 35] Furthermore, some studies suggest that pregnancy ambivalence itself is an independent risk factor for low birth weight.[33, 36, 37]

Based on population data, rheumatologists need to anticipate that a subset of women living with lupus will have ambivalence about pregnancy. Unfortunately, in women with lupus, pregnancy ambivalence can be particularly risky given the importance of timing conception to coincide with periods of low lupus disease activity, continuing pregnancy-compatible medications, and avoiding conception when taking a teratogen. These patients additionally need to engage in the routine healthy behaviors for pregnancy such as taking a prenatal multivitamin and avoiding alcohol. It is clear from this cohort that women with lupus who were ambivalent about pregnancy were not sufficiently addressing these risks. In particular, none of the women ambivalent about pregnancy were regularly using contraception, despite many of them having very active lupus and/or taking a teratogen.

A systematic review and meta-analysis by LaCross et al. demonstrated that women who are ambivalent about pregnancy are 2.41 times more likely to not use contraception.[38] Additionally, qualitative approaches have highlighted the impacts of pregnancy ambivalence in the type of contraception that patients choose for themselves. Specifically, long-acting reversible contraceptive methods (intrauterine devices and implants) were seen as too “permanent” among many women who were ambivalent about pregnancy, despite acknowledging that they were removable at any time.[39] Ambivalence about pregnancy also increases the likelihood of women engaging in high-risk behaviors during pregnancy. Specifically, these women are less likely to receive prenatal care, less likely to take folic acid or multivitamins, and more likely to smoke at baseline and during pregnancy.[40-42]

Counseling for ambivalent women and those who do not intend pregnancy may help improve contraception use. Systematic review by Oringanje et al. has recommended a combination of educational and contraceptive-promoting interventions to help decrease unintended pregnancies.[44] In another high-risk population, women with HIV, patients were at lower risk for having an unplanned or ambivalent pregnancy if they had a discussion of their pregnancy intentions with their provider prior to pregnancy.[21] Provider-initiated questions can be somewhat helpful as demonstrated by the success of the One Key Question (OKQ), “Would you like to become pregnant in the next year?”[43] While the OKQ opens the door for conversations on pregnancy intention, a limitation is that it can be interpreted as a “yes” or “no” question and may not pick up the ambivalence towards pregnancy that some women experience.[43] Although this is an area for future research, an open-ended approach to evaluating pregnancy intention will likely allow for better characterization of pregnancy intention and the reasons underlying ambivalence. Furthermore, we hypothesize that addressing pregnancy ambivalence can be an effective approach to encouraging planned pregnancies in lupus.

Pre-pregnancy counseling can help women with lupus who desire pregnancy conceive during periods of low disease activity, thereby helping to improve outcomes. Counseling can also support these patients in safely switching to pregnancy-compatible lupus medications and continuing them through the duration of pregnancy. In this study, the rates of pre-pregnancy counseling with a rheumatologist were higher among planned lupus pregnancies as compared to not-planned pregnancies; however, even among planned pregnancies, almost half the women did not receive counseling despite receiving care at a tertiary medical center. This suggests that there is a need for improved pre-pregnancy counseling among reproductive-aged women with lupus. Similarly, women with not-planned pregnancies were more likely to discontinue and require newly starting or restarting pregnancy-compatible lupus medications. Our data suggests that adherence to these medications may need to be improved in both groups. Lastly, while the overall rate of prenatal vitamin use in this cohort (49%) was consistent with women in other western countries (20-53%) and higher than women with HIV (13%), only one woman with a not-planned lupus pregnancy reported prenatal vitamin use.[18, 20, 21, 45] Medication data from this study highlights the necessity of encouraging multivitamin use and adherence to appropriate pregnancy-compatible medications, in particular hydroxychloroquine and azathioprine, in all reproductive-aged women with lupus, regardless of stated pregnancy intention.[4, 46]

Limitations of this study include small sample size, especially with regards to pregnancy outcomes; however, to date, this is the largest cohort of lupus pregnancies with data on pregnancy intention. Additionally, this cohort only included lupus patients in the Southeastern United States and there might be demographic differences to consider when generalizing the conclusions. Lastly, not all pregnancy planning behaviors as documented by the LMUP survey were able to be interpreted as information regarding baseline tobacco use, alcohol use, and pre-pregnancy diet was unavailable.

In conclusion, in this prospective cohort, ambivalence regarding pregnancy was associated higher clinical and behavioral risk factors, as well as higher rates of severe pregnancy and neonatal outcomes. While we have known for decades that conceiving when lupus has been active or when taking a teratogen places the pregnancy at higher risk, this is the first study to identify pregnancy intention as a potentially modifiable risk factor for poor outcomes in women with lupus. Studies outside of rheumatology demonstrate that addressing pregnancy ambivalence can improve contraceptive use and increase appropriate pregnancy planning behaviors. We suggest that proactive, collaborative, and empathetic pregnancy planning by rheumatologists may be the best way to improve outcomes in these high-risk pregnancies. Our group's efforts to improve patient-provider communication have identified gaps in rheumatologists' knowledge and ability to provide adequate pregnancy planning for lupus patients.[47] We believe rheumatologists can play a larger role in assisting their patients with lupus decrease ambivalence about pregnancy by initiating open and honest conversations about reproductive health. With this goal in mind, we have created a website and handout to aid rheumatologists in following the ACR's Reproductive Health Guideline to guide contraceptive use and pregnancy planning more effectively (www.lupuspregnancy.org).[48] By partnering with women with lupus to plan for pregnancy, rheumatologists have the opportunity to decrease the short-term and long-term maternal-fetal morbidity and mortality associated with lupus pregnancies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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TABLE 1:

DEMOGRAPHICS AND COMORBIDITIES

DEMOGRAPHICS	**Overall N=43**	**Not-Planned n=17**	**Planned n=26**	**p-value**
Maternal Age, years (mean ± S.D.)	29.4 ± 5.4	26.5 ± 5.3	31.3 ± 4.6	0.005
Maternal Race:				
Black	18 (42%)	9 (53%)	9 (35%)	0.5
White	16 (37%)	5 (29%)	11 (42%)	
Other	9 (21%)	3 (18%)	6 (23%)	
Maternal Ethnicity: Hispanic	4 (9%)	2 (12%)	2 (8%)	1.0
Education Level: Less than college	16 (37%)	12 (71%)	4 (15%)	0.0004
Marital Status: Single	9 (21%)	7 (41%)	2 (8%)	0.02
Living situation: Alone or with children	4 (9%)	2 (12%)	2 (8%)	1.0
Health Insurance: Medicaid	15 (35%)	11 (65%)	4 (15%)	0.003
Annual Income: < $50,000	14/40 (35%)	11/17 (65%)	3/23 (13%)	0.002
Annual Income: > $150,000	6/40 (15%)	2/17 (12%)	4/23 (17%)	1.0
COMORBIDITIES	**Overall**	**Not-planned**	**Planned**	**p-value**
Chronic Hypertension	10 (23%)	4 (24%)	6 (23%)	1.0
Diabetes Mellitus	0 (0%)	0 (0%)	0 (0%)	--
Antiphospholipid Syndrome	3 (7%)	1 (6%)	2 (8%)	1.0
PRE-PREGNANCY LUPUS ACTIVITY				
PGA (mean ± S.D.)	0.6 ± 0.6	1.0 ± 0.6	0.3 ± 0.5	0.001

TABLE 2:

LMUP SURVEY DATA

LMUP SURVEY DATA	Overall N=43	Not-planned n=17	Planned n=26	p-value
LMUP Total Score (mean ± S.D.)	9.2 ± 2.9	5.9 ± 1.8	11.3 ± 0.8	<0.0001
Not using contraception[1]	39 (91%)	13 (76%)	26 (100%)	0.02
Sometimes using contraception / known contraception failure	4 (9%)	4 (24%)	0 (0%)	
Always using contraception	0 (0%)	0 (0%)	0 (0%)	
Right time for pregnancy[1]	25 (58%)	2 (12%)	23 (88%)	< 0.0001
Not quite right time for pregnancy	16 (37%)	13 (76%)	3 (12%)	
Wrong time for pregnancy	2 (5%)	2 (12%)	0 (0%)	
Intended pregnancy[1]	24 (56%)	2 (12%)	22 (85%)	< 0.0001
Changing pregnancy intentions	9 (21%)	6 (35%)	3 (12%)	
Unintended pregnancy	10 (23%)	9 (53%)	1 (4%)	
Wanted to have a baby[1]	29 (67%)	4 (24%)	25 (96%)	< 0.0001
Mixed feelings	11 (26%)	10 (59%)	1 (4%)	
Did not want to have a baby	3 (7%)	3 (18%)	0 (0%)	
Agreed on pregnancy with partner[1]	30 (70%)	4 (24%)	26 (100%)	< 0.0001
Discussed with partner but did not agree	11 (26%)	11 (65%)	0 (0%)	
Never discussed having children with partner	2 (5%)	2 (12%)	0 (0%)	
2 or more planning behaviors[1]	20 (47%)	2 (12%)	18 (69%)	0.0004
1 planning behavior	9 (21%)	3 (18%)	6 (23%)	
No planning behaviors	14 (33%)	12 (71%)	2 (8%)	

1. p-value comparisons between not-planned and planned pregnancies were performed for the statements which correspond to having a planned pregnancy.

TABLE 3:

PREGNANCY PLANNING BEHAVIORS

LMUP PLANNING BEHAVIORS	Overall N=43	Not-planned n=17	Planned n=26	p-value
Changed medications for rheumatic disease[1]	7 (16%)	0 (0%)	7 (27%)	0.03
Sought medical or health advice	11 (26%)	2 (12%)	9 (35%)	0.2
Took prenatal vitamins or folic acid	21 (49%)	1 (6%)	20 (77%)	< 0.0001
Stopped or cut down on alcohol[2]	12 (28%)	2 (12%)	10 (38%)	0.08
Stopped or cut down on smoking[2]	3 (7%)	1 (6%)	2 (8%)	1.0
Ate more healthily	12 (28%)	2 (12%)	10 (38%)	0.08
Took some other action:				
Exercise	1 (2%)	0 (0%)	1 (4%)	--
Weight Loss	1 (2%)	0 (0%)	1 (4%)	--
Did none of the above prior to pregnancy	14 (33%)	12 (71%)	2 (8%)	< 0.0001
PRE-PREGNANCY COUNSELING	**Overall**	**Not-planned**	**Planned**	**p-value**
Received with Rheumatology	18/42 (43%)	3/16 (19%)	15/26 (58%)	0.02
Recommended OK to conceive	12/17 (71%)	0/2 (0%)	12/15 (80%)	0.07

1. This statement was not a part of the original LMUP survey and was added when survey was administered to this cohort of patients.

2. The LMUP survey does not include questions on baseline levels of smoking and alcohol use.

TABLE 4:

COMPOSITE DELIVERY OUTCOMES

PREGNANCY PLANNING [1]	**Overall N=35**	**Not-planned n=15**	**Planned n=20**	**p-value**
PROMISSE-APO[2]	20/33 (61%)	11/14 (79%)	9/19 (47%)	0.09
Severe PROMISSE-APO[3]	6/33 (18%)	6/14 (43%)	0/19 (0%)	0.003
Severe Neonatal Outcome[4]	13/29 (45%)	7/10 (70%)	6/19 (32%)	0.06
PRE-PREGNANCY LUPUS ACTIVITY[1]	**Overall N=35**	**PGA ≥ 1.5 n=6**	**PGA < 1.5 n=29**	**p-value**
PROMISSE-APO[2]	20/33 (61%)	5/5 (100%)	15/28 (54%)	0.1
Severe PROMISSE-APO[3]	6/33 (18%)	3/5 (60%)	3/28(11%)	0.03
Severe Neonatal Outcome[4]	13/29 (45%)	4/4 (100%)	9/25 (36%)	0.03
MATERNAL RACE[5]	**Overall N=35**	**Black n=15**	**White or Other n=20**	**p-value**
PROMISSE-APO[2]	20/33 (61%)	10/14 (71%)	10/19 (53%)	0.3
Severe PROMISSE-APO[3]	6/33 (18%)	4/14 (29%)	2/19(11%)	0.4
Severe Neonatal Outcome[4]	13/29 (45%)	6/11 (55%)	7/18 (39%)	0.5

1. Delivery outcomes missing: 8 pregnancies; not delivered as of 4/1/2020 (n=7) or data was unavailable (n=1).

2. PROMISSE-APO: neonatal death, fetal death > 12 weeks, preeclampsia, preterm delivery < 36 weeks, or small for gestational age (SGA) < 5th percentile. Pregnancy losses < 12 weeks were excluded.[10]

3. Severe PROMISSE-APO: neonatal death, fetal death > 12 weeks, preeclampsia and preterm delivery < 34 weeks, or preterm delivery < 30 weeks. Pregnancy losses < 12 weeks were excluded.[10]

4. Severe neonatal outcomes among live births: neonatal death, NICU stay > 1 week, APGAR < 7 at 5 minutes, or SGA < 5th percentile.

5. For composite delivery outcomes by demographics, see Supplemental Table 2.

TABLE 5:

DISEASE ACTIVITY AND HOSPITAL VISITS

DISEASE ACTIVITY	**Overall N=35**	**Not-planned n=15**	**Planned n=20**	**p-value**
Max. lupus activity (PGA) (mean ± S.D.)[1]	0.8 ± 0.7	1.1 ± 0.8	0.6 ± 0.7	0.05
Prednisone use > 7.5 mg/day	14 (40%)	9 (60%)	5 (25%)	0.08
HOSPITAL VISITS	**Overall**	**Not-planned**	**Planned**	**p-value**
Patients requiring a visit outside of delivery[2]	19 (54%)	12 (80%)	7 (35%)	0.02
Number of visits	40	24	16	
Number of visits (mean ± S.D.)[3]	1.1 ± 1.4	1.6 ± 1.2	0.8 + 1.4	0.08
Length of stay per patient (median and IQR)[4]	2.8 (1.5-6.0)	2.8 (1.5-7.8)	2.5 (1.5-3.0)	0.9
LUPUS-RELATED HOSPITAL VISITS	**Overall**	**Not-planned**	**Planned**	**p-value**
Patients requiring a visit outside of delivery	7 (20%)	5 (33%)	2 (10%)	0.1
Number of visits	11	8	3	
Number of visits (mean ± S.D.)[3]	0.3 ± 0.7	0.5 ± 0.8	0.2 ± 0.5	0.1

1. Maximum lupus activity in pregnancy (PGA) was missing in 1 pregnancy.

2. Includes any hospital visit (lupus-related and non-lupus related) for reason other than delivery. Lupus-related hospital visits included CNS lupus, lupus nephritis, pericarditis, serositis, hemolytic anemia, pancytopenia, and worsening pulmonary hypertension. Reasons for non-lupus-related hospital visits include chronic hypertension, asthma, infections, musculoskeletal chest pain, fetal heart block, preeclampsia rule-out, preterm labor rule-out, vaginal bleeding, and symptoms such as edema, nausea, vomiting, and abdominal cramping.

3. Number of visits (mean ± S.D.) calculated out of all patients, including those who did not have a hospital visit during pregnancy.

4. Length of stay calculated out of only patients who had a hospital visit. Hospital visits with length of stay < 1 day were considered as 0.5 days.

TABLE 6:

MEDICATIONS

PERICONCEPTIONAL PERIOD	Overall N=43	Not-planned n=17	Planned n=26	p-value
Discontinued pregnancy-compatible medication:				
Any lupus medication[1]	10/38 (26%)	6/13 (46%)	4/25 (16%)	0.06
Corticosteroid	2/11 (18%)	1/4 (25%)	1/7 (14%)	1.0
Hydroxychloroquine	4/37(11%)	4/13 (31%)	0/24 (0%)	0.01
Azathioprine	4/12 (33%)	2/3 (67%)	2/9 (22%)	0.2
Continued pregnancy-compatible medication:				
Any lupus medication[2]	35/38 (92%)	10/13 (77%)	25/25 (100%)	0.03
Corticosteroid	9/11 (82%)	3/4 (75%)	6/7 (86%)	1.0
Hydroxychloroquine	33/37 (89%)	9/13 (69%)	24/24 (100%)	0.01
Azathioprine	8/12 (67%)	1/3 (33%)	7/9 (78%)	0.2
DURING PREGNANCY[3]	**Overall N=35**	**Not-planned n=15**	**Planned n=20**	**p-value**
Started pregnancy-compatible medication in pregnancy:				
Any lupus medication[4]	21/35 (60%)	15/15 (100%)	6/20 (30%)	<0.0001
Corticosteroid	13/29 (45%)	8/12 (67%)	5/17 (29%)	0.07
Hydroxychloroquine	8/9 (89%)	7/7 (100%)	1/2 (50%)	0.2
Azathioprine	12/29 (41%)	8/14 (57%)	4/15 (27%)	0.1

1. Discontinued ≥1 pregnancy-compatible lupus medication in the three months prior to and following conception.

2. Continued ≥1 pregnancy-compatible lupus medication in the three months prior to and following conception.

3. Medication use during pregnancy excluded patients with unavailable delivery outcomes (n=8) as of 4/1/2020.

4. Required newly starting or re-starting ≥1 pregnancy-compatible medication during pregnancy.