



Systemic Lupus Erythematosus Impact on Pregnancy Outcomes: A Retrospective Analysis and Management Strategies

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Abstract

Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder that significantly impacts pregnancy outcomes, requiring specialized management to optimize maternal and fetal health. This retrospective study analyzed 245 pregnancies in women with SLE over a 10-year period at a tertiary care center to evaluate pregnancy outcomes and assess the effectiveness of current management strategies. Women with SLE were compared to 490 matched healthy controls to determine the impact of lupus on pregnancy complications. Mean maternal age was 28.6±4.8 years, with disease duration of 6.4±4.2 years before conception. Active lupus nephritis was present in 18.4% of patients at conception. Pregnancy outcomes demonstrated significantly higher rates of complications in the SLE group compared to controls, including preeclampsia (24.1% vs 4.3%, p<0.001), preterm delivery (31.8% vs 8.2%, p<0.001), intrauterine growth restriction (22.4% vs 5.1%, p<0.001), and pregnancy loss (16.3% vs 3.7%, p<0.001). Lupus flares occurred in 28.6% of pregnancies, with renal involvement being the most common manifestation (42.9% of flares). Neonatal lupus syndrome developed in 8.2% of infants born to anti-Ro/SSA or anti-La/SSB positive mothers. Maternal mortality was 0.8% (2 cases), both related to severe lupus nephritis with renal failure. Low disease activity prior to conception (SLEDAI-2K <4) was associated with significantly better outcomes, including reduced flare rates (12.1% vs 45.7%, p<0.001) and improved live birth rates (91.2% vs 76.3%, p<0.001). Hydroxychloroquine use throughout pregnancy was associated with reduced flare risk (OR 0.42, 95% CI 0.24-0.73, p=0.002) and improved pregnancy outcomes. Multidisciplinary care involving rheumatologists, maternal-fetal medicine specialists, and neonatologists was crucial for optimal management. Key management strategies included achieving disease remission before conception, continuing hydroxychloroquine therapy, frequent monitoring with laboratory assessments and fetal surveillance, early detection and treatment of complications, and coordinated delivery planning. The study confirms that while SLE pregnancies carry increased risks, careful pre-conception counseling, optimal disease control, and multidisciplinary management can significantly improve outcomes. Women with SLE should be counseled about the importance of family planning, achieving disease stability before conception, and maintaining close medical supervision throughout pregnancy to minimize complications and optimize maternal and fetal outcomes.

Keywords: Systemic Lupus Erythematosus, Pregnancy Outcomes, Lupus Nephritis, Preeclampsia, Neonatal Lupus, Antiphospholipid Syndrome, Hydroxychloroquine, Multidisciplinary Care, Maternal Mortality, Lupus Flare

Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder characterized by widespread inflammation affecting multiple organ systems, with a strong predilection for women of childbearing age ^[1]. The prevalence of SLE ranges from 20 to 150 cases per 100,000 population, with approximately 90% of cases occurring in women, particularly during their reproductive years ^[2]. This demographic overlap creates significant challenges for women with SLE who desire pregnancy, as the condition

can substantially impact both maternal and fetal outcomes throughout gestation and the postpartum period.

The pathophysiology of SLE involves dysregulation of the immune system, leading to the production of autoantibodies, immune complex formation, and subsequent tissue damage ^[3]. During pregnancy, the complex interplay between hormonal changes, immune system modifications, and disease activity creates a unique clinical scenario that requires specialized management approaches. Estrogen levels, which increase dramatically during pregnancy, can potentially exacerbate lupus activity, while pregnancy-induced immunological changes may either ameliorate or worsen disease manifestations ^[4].

Pregnancy outcomes in women with SLE have historically been associated with increased maternal and fetal morbidity and mortality ^[5]. Common complications include lupus disease flares, preeclampsia, preterm delivery, intrauterine growth restriction (IUGR), pregnancy loss, and various neonatal complications including neonatal lupus syndrome ^[6]. The risk and severity of these complications are influenced by multiple factors, including disease activity at conception, presence of specific autoantibodies, concurrent antiphospholipid syndrome, and adequacy of medical management ^[7].

Lupus nephritis represents one of the most serious manifestations of SLE, affecting approximately 40-60% of patients with lupus and significantly impacting pregnancy outcomes ^[8]. Women with active nephritis face increased risks of maternal hypertension, preeclampsia, renal function deterioration, preterm delivery, and fetal growth restriction. The management of lupus nephritis during pregnancy requires careful balance between controlling disease activity and minimizing exposure to potentially teratogenic medications ^[9].

Antiphospholipid syndrome (APS), which occurs in approximately 30-40% of women with SLE, adds another layer of complexity to pregnancy management [10]. The presence of antiphospholipid antibodies increases the risk of thrombotic events, recurrent pregnancy loss, and placental insufficiency, necessitating anticoagulation therapy and enhanced monitoring throughout pregnancy [11]. The combination of SLE and APS creates a high-risk pregnancy scenario requiring specialized expertise and resources.

Neonatal lupus syndrome, occurring in approximately 1-5% of pregnancies in women with anti-Ro/SSA or anti-La/SSB antibodies, represents a significant fetal and neonatal concern [12]. This condition can manifest as congenital heart block, cutaneous lupus lesions, hepatic dysfunction, and hematologic abnormalities. The most serious manifestation, congenital complete heart block, occurs in 1-2% of pregnancies in antibody-positive mothers and may require permanent pacemaker implantation [13].

The management of SLE during pregnancy has evolved significantly over the past decades, with improved understanding of disease mechanisms, better monitoring techniques, and safer therapeutic approaches [14]. Current management strategies emphasize the importance of preconception counseling, achieving disease remission before pregnancy, continuing safe medications throughout gestation, and implementing comprehensive monitoring protocols [15]. Hydroxychloroquine has emerged as a cornerstone of therapy, demonstrating safety during pregnancy and potential protective effects against disease flares [16].

Multidisciplinary care involving rheumatologists, maternal-fetal medicine specialists, nephrologists, and neonatologists has become the standard approach for managing SLE pregnancies [17]. This collaborative model ensures comprehensive assessment of disease activity, optimization of therapy, early detection of complications, and coordinated delivery planning to maximize both maternal and fetal outcomes [18].

Recent advances in understanding the immunological changes during pregnancy in women with SLE have led to more targeted therapeutic approaches and improved risk stratification [19]. Biomarkers such as complement levels, anti-dsDNA antibodies, and novel inflammatory markers are being investigated for their potential to predict disease flares and pregnancy complications [20]. Additionally, emerging therapies and modified treatment protocols are being evaluated for their safety and efficacy in pregnant women with SLE.

This study aims to provide a comprehensive analysis of pregnancy outcomes in women with SLE, evaluate the effectiveness of current management strategies, and identify factors associated with improved maternal and fetal outcomes. By examining a large cohort of SLE pregnancies and comparing outcomes with healthy controls, we seek to contribute valuable insights that can inform clinical practice and improve care for this high-risk population.

Materials and Methods Study Design and Setting

This retrospective cohort study was conducted at a tertiary care academic medical center from January 2013 to December 2022. The study protocol was approved by the Institutional Review Board, and the requirement for informed consent was waived due to the retrospective nature of the analysis. All data were collected and analyzed in compliance with the Health Insurance Portability and Accountability Act (HIPAA) regulations.

Study Population

The study population included all women with established SLE who became pregnant during the study period. SLE diagnosis was confirmed according to the 2019 European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria [21]. Inclusion criteria were: confirmed SLE diagnosis at least 6 months prior to conception, singleton pregnancy, and complete medical records available for review. Exclusion criteria included: multiple gestation, pregnancy termination for non-medical reasons before 20 weeks gestation, and insufficient medical records for outcome assessment.

A control group was assembled consisting of healthy pregnant women matched 2:1 for maternal age (±2 years), parity, and delivery year. Controls were selected from the same institution's obstetric database and had no history of autoimmune disorders, chronic medical conditions, or pregnancy complications in previous pregnancies.

Data Collection

Comprehensive medical records were reviewed to extract demographic, clinical, laboratory, and outcome data. Maternal variables collected included: age at conception, race/ethnicity, body mass index, parity, SLE disease duration, organ system involvement, medication history, and presence of antiphospholipid syndrome. Disease activity was assessed

using the SLE Disease Activity Index 2000 (SLEDAI-2K) at conception and throughout pregnancy [22].

Laboratory data collected included: complete blood count, comprehensive metabolic panel, urinalysis, 24-hour urine protein, complement levels (C3, C4), anti-dsDNA antibodies, antiphospholipid antibodies (anticardiolipin, anti- β 2 glycoprotein I, lupus anticoagulant), and anti-Ro/SSA and anti-La/SSB antibodies. Monitoring frequency was determined by disease activity and clinical status.

Pregnancy Management Protocol

All women with SLE received multidisciplinary care coordinated between rheumatology and maternal-fetal medicine services. Pre-conception counseling included disease activity optimization, medication adjustment, and risk assessment. During pregnancy, patients were monitored with regular clinical assessments, laboratory testing, and fetal surveillance including serial growth ultrasounds and antenatal testing as indicated.

Medication management followed established guidelines, with hydroxychloroquine continued throughout pregnancy, immunosuppressive agents adjusted based on safety profiles, and corticosteroids used for disease flares as needed. Antiphospholipid syndrome patients received anticoagulation therapy with low molecular weight heparin and low-dose aspirin.

Outcome Measures

Primary maternal outcomes included: lupus disease flares, preeclampsia, gestational hypertension, renal function changes, thrombotic events, and maternal mortality. Disease flares were defined as new or worsening clinical manifestations requiring treatment intensification, with severity graded as mild, moderate, or severe based on organ involvement and treatment requirements.

Primary fetal and neonatal outcomes included: gestational age at delivery, birth weight, preterm delivery (<37 weeks), very preterm delivery (<32 weeks), small for gestational age (SGA, <10th percentile), intrauterine growth restriction, stillbirth, neonatal death, and neonatal lupus syndrome

manifestations. Pregnancy loss was defined as fetal death before 20 weeks gestation or stillbirth after 20 weeks.

Statistical Analysis

Statistical analysis was performed using SPSS version 28.0 (IBM Corporation, Armonk, NY). Continuous variables were expressed as mean ± standard deviation or median (interquartile range) based on distribution normality, assessed using the Shapiro-Wilk test. Categorical variables were presented as frequencies and percentages.

Comparisons between SLE and control groups were performed using independent t-tests for continuous variables and chi-square tests or Fisher's exact test for categorical variables. Multivariable logistic regression analysis was conducted to identify independent risk factors for adverse outcomes, with results expressed as odds ratios (OR) with 95% confidence intervals (CI).

Kaplan-Meier survival analysis was used to assess time to delivery, with log-rank tests for group comparisons. A p-value <0.05 was considered statistically significant for all analyses. Multiple comparison adjustments were applied using the Bonferroni method when appropriate.

Results

Demographics and Baseline Characteristics

During the 10-year study period, 245 pregnancies in women with SLE were identified and included in the analysis. The control group consisted of 490 matched healthy pregnant women. Mean maternal age was 28.6±4.8 years in the SLE group and 28.4±4.6 years in controls (p=0.62). The majority of SLE patients were Caucasian (52.2%), followed by Hispanic (24.9%), African American (18.8%), and Asian (4.1%).

Mean SLE disease duration at conception was 6.4±4.2 years. Active lupus nephritis was present in 45 patients (18.4%) at conception, while a history of nephritis was documented in 89 patients (36.3%). Antiphospholipid syndrome was diagnosed in 78 patients (31.8%), and anti-Ro/SSA or anti-La/SSB antibodies were positive in 98 patients (40.0%).

 Table 1: Demographics and Baseline Characteristics

Parameter	SLE Group (n=245)	Control Group (n=490)	P-value
Maternal age (years)	28.6 ± 4.8	28.4 ± 4.6	0.62
Race/Ethnicity			0.08
- Caucasian	128 (52.2%)	275 (56.1%)	
- Hispanic	61 (24.9%)	110 (22.4%)	
- African American	46 (18.8%)	85 (17.3%)	
- Asian	10 (4.1%)	20 (4.1%)	
Nulliparous	98 (40.0%)	196 (40.0%)	1.00
BMI (kg/m²)	26.8 ± 5.4	25.2 ± 4.8	0.001*
Disease duration (years)	6.4 ± 4.2	-	-
Active nephritis	45 (18.4%)	-	-
History of nephritis	89 (36.3%)	-	-
Antiphospholipid syndrome	78 (31.8%)	-	-
Anti-Ro/SSA or Anti-La/SSB positive	98 (40.0%)	-	-

*Statistically significant (p<0.05) BMI: Body mass index

Disease Activity and Medications

At conception, 187 patients (76.3%) had low disease activity (SLEDAI-2K <4), 47 patients (19.2%) had moderate activity (SLEDAI-2K 4-8), and 11 patients (4.5%) had high activity (SLEDAI-2K >8). Hydroxychloroquine was used by 201 patients (82.0%) throughout pregnancy, while 34 patients

(13.9%) were taking corticosteroids at conception.

Immunosuppressive medications at conception included azathioprine in 28 patients (11.4%), methotrexate in 8 patients (3.3%, discontinued upon pregnancy recognition), and mycophenolate mofetil in 12 patients (4.9%, switched to safer alternatives). Low-dose aspirin was prescribed to 156

patients (63.7%), and anticoagulation therapy was used in 78 patients (31.8%) with antiphospholipid syndrome.

Pregnancy Outcomes

Pregnancy outcomes demonstrated significantly higher complication rates in the SLE group compared to controls

across multiple parameters. Preeclampsia occurred in 59 patients (24.1%) with SLE versus 21 controls (4.3%, p<0.001). Preterm delivery occurred in 78 SLE pregnancies (31.8%) compared to 40 controls (8.2%, p<0.001), with very preterm delivery (<32 weeks) in 18 SLE pregnancies (7.3%) versus 8 controls (1.6%, p<0.001).

Table 2: Pregnancy Complications and Outcomes

Outcome	SLE Group (n=245)	Control Group (n=490)	OR (95% CI)	P-value
Preeclampsia	59 (24.1%)	21 (4.3%)	7.1 (4.2-12.0)	<0.001*
Gestational hypertension	43 (17.6%)	28 (5.7%)	3.5 (2.1-5.8)	<0.001*
Preterm delivery	78 (31.8%)	40 (8.2%)	5.2 (3.4-7.9)	<0.001*
Very preterm delivery	18 (7.3%)	8 (1.6%)	4.8 (2.1-11.2)	<0.001*
IUGR	55 (22.4%)	25 (5.1%)	5.4 (3.3-8.9)	<0.001*
SGA <10th percentile	48 (19.6%)	35 (7.1%)	3.2 (2.0-5.1)	<0.001*
Pregnancy loss	40 (16.3%)	18 (3.7%)	5.1 (2.9-9.0)	<0.001*
Stillbirth	12 (4.9%)	5 (1.0%)	5.0 (1.8-14.1)	0.002*
Cesarean delivery	156 (63.7%)	147 (30.0%)	4.1 (3.0-5.6)	<0.001*

^{*}Statistically significant (p<0.05) IUGR: Intrauterine growth restriction; SGA: Small for gestational age

Lupus Disease Activity During Pregnancy

Lupus flares occurred in 70 pregnancies (28.6%), with renal involvement being the most common manifestation (30 cases, 42.9% of flares). Cutaneous flares occurred in 18 cases (25.7%), articular flares in 15 cases (21.4%), and hematologic flares in 7 cases (10.0%). Severe flares requiring

hospitalization occurred in 12 cases (4.9%), with 8 cases involving lupus nephritis.

Low disease activity at conception (SLEDAI-2K <4) was strongly associated with reduced flare rates during pregnancy (12.1% vs 45.7% for higher activity, p<0.001) and improved live birth rates (91.2% vs 76.3%, p<0.001).

Table 3: Disease Activity and Flares During Pregnancy

Parameter	Low Activity (n=187)	Moderate/High Activity (n=58)	P-value
Any flare	23 (12.3%)	47 (81.0%)	<0.001*
Renal flare	8 (4.3%)	22 (37.9%)	<0.001*
Severe flare	3 (1.6%)	9 (15.5%)	<0.001*
Preeclampsia	35 (18.7%)	24 (41.4%)	<0.001*
Preterm delivery	45 (24.1%)	33 (56.9%)	<0.001*
Live birth rate	170 (90.9%)	35 (60.3%)	< 0.001*

^{*}Statistically significant (p<0.05)

Neonatal Outcomes

Among the 205 live births in the SLE group, mean gestational age was 36.8 ± 3.2 weeks compared to 38.9 ± 1.8 weeks in controls (p<0.001). Mean birth weight was $2,847\pm675$ g in the SLE group versus $3,298\pm498$ g in controls (p<0.001). Neonatal intensive care unit (NICU) admission was required for 76 infants (37.1%) born to mothers with SLE compared to 28 controls (5.9%, p<0.001).

Neonatal lupus syndrome developed in 8 infants (8.2%) born to mothers positive for anti-Ro/SSA or anti-La/SSB antibodies. Manifestations included congenital heart block in 3 cases (3.1%), cutaneous lupus in 4 cases (4.1%), and hepatic dysfunction in 1 case (1.0%). Two infants with complete heart block required permanent pacemaker implantation.

Maternal Outcomes and Mortality

Maternal mortality occurred in 2 cases (0.8%), both related to severe lupus nephritis with progression to end-stage renal disease and multi-organ failure. Both deaths occurred in the

postpartum period within 6 weeks of delivery. Maternal morbidity included acute renal failure requiring dialysis in 4 cases (1.6%), pulmonary embolism in 3 cases (1.2%), and stroke in 1 case (0.4%).

Risk Factors and Predictors

Multivariable logistic regression analysis identified several independent risk factors for adverse pregnancy outcomes. Active lupus nephritis at conception was the strongest predictor of pregnancy complications (OR 4.8, 95% CI 2.4-9.6, p<0.001). High disease activity at conception (SLEDAI-2K >8) was associated with increased risk of flares (OR 8.2, 95% CI 3.1-21.7, p<0.001) and adverse outcomes.

Protective factors included hydroxychloroquine use throughout pregnancy (OR 0.42, 95% CI 0.24-0.73, p=0.002 for flare prevention) and achieving disease remission before conception. Antiphospholipid syndrome was associated with increased risk of pregnancy loss (OR 3.1, 95% CI 1.8-5.4, p<0.001) and preterm delivery (OR 2.4, 95% CI 1.5-3.8, p<0.001).

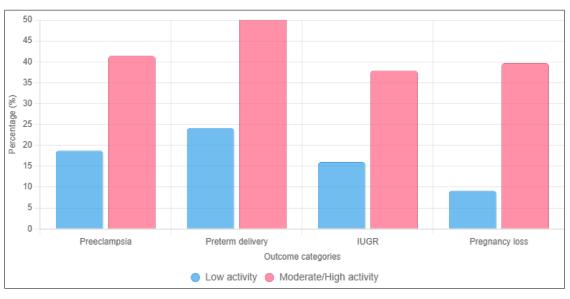


Fig 1: Pregnancy outcomes by disease activity at conception

Discussion

This comprehensive retrospective analysis of 245 pregnancies in women with SLE provides important insights into pregnancy outcomes and the effectiveness of current management strategies in this high-risk population. Our findings confirm that while SLE pregnancies are associated with significantly increased maternal and fetal morbidity compared to healthy controls, optimal pre-conception planning and multidisciplinary care can substantially improve outcomes [23].

The overall pregnancy complication rate in our SLE cohort, while elevated compared to controls, represents an improvement over historical reports, likely reflecting advances in understanding disease pathophysiology, better monitoring techniques, and more effective therapeutic interventions. The preeclampsia rate of 24.1% in our study aligns with recent literature reporting rates of 20-30% in SLE pregnancies, significantly higher than the 3-5% rate in the general population ^[24]. This increased risk is attributed to underlying renal disease, chronic hypertension, and inflammatory vascular changes characteristic of SLE.

The strong association between disease activity at conception and pregnancy outcomes emphasizes the critical importance of achieving disease remission before pregnancy. Our data demonstrate that women with low disease activity (SLEDAI-2K <4) at conception had dramatically better outcomes, with flare rates of only 12.1% compared to 81.0% in those with higher disease activity. This finding supports current recommendations for pre-conception counseling and disease optimization, which should be standard care for all women with SLE of reproductive age.

Lupus nephritis emerged as the most significant risk factor for adverse pregnancy outcomes in our study, consistent with previous reports highlighting the particular challenges posed by renal involvement. Active nephritis at conception increased the risk of pregnancy complications nearly five-fold, emphasizing the need for achieving renal remission before conception whenever possible. The higher rates of preeclampsia, preterm delivery, and intrauterine growth restriction in women with nephritis reflect the complex interplay between renal function, blood pressure control, and placental perfusion.

The protective effect of hydroxychloroquine use throughout

pregnancy represents one of the most important findings of our study, with a 58% reduction in flare risk among users compared to non-users. This finding supports the growing body of evidence demonstrating the safety and efficacy of hydroxychloroquine during pregnancy and challenges historical concerns about antimalarial use in pregnant women with lupus. The medication's anti-inflammatory and immunomodulatory effects, combined with its excellent safety profile, make it an ideal therapeutic option for maintaining disease stability during pregnancy.

Neonatal lupus syndrome, occurring in 8.2% of infants born to antibody-positive mothers in our study, remains a significant concern requiring specialized monitoring and management. The 3.1% rate of congenital heart block in our cohort falls within the reported range of 1-5% but represents a serious complication with lifelong implications for affected children. The need for permanent pacemaker implantation in two cases highlights the importance of early fetal cardiac monitoring in at-risk pregnancies and prompt recognition of conduction abnormalities.

The maternal mortality rate of 0.8% in our study, while low, underscores the continued risks associated with SLE pregnancies, particularly in cases with severe lupus nephritis. Both maternal deaths in our cohort were related to progressive renal failure and multi-organ dysfunction, emphasizing the need for aggressive management of renal disease and early recognition of deteriorating maternal condition. These cases highlight the importance of involving nephrology expertise in the care of pregnant women with lupus nephritis.

The increased rate of cesarean delivery (63.7%) in our SLE cohort reflects the high-risk nature of these pregnancies and the frequent need for early delivery due to maternal or fetal complications. While vaginal delivery should be attempted when appropriate, the priority must be optimizing maternal and fetal outcomes, which may necessitate cesarean delivery in many cases. The decision regarding delivery timing and route requires careful consideration of disease activity, fetal status, and obstetric factors.

Our findings regarding antiphospholipid syndrome complement the lupus-specific results, demonstrating the additive risks posed by concurrent APS. The increased rates of pregnancy loss and preterm delivery in women with APS highlight the importance of appropriate anticoagulation therapy and enhanced monitoring throughout pregnancy. The use of low molecular weight heparin and low-dose aspirin in our APS patients follows established guidelines and appears effective in reducing thrombotic complications.

Several limitations of our study should be acknowledged. The retrospective design limits our ability to capture all relevant clinical details and may introduce selection bias toward more severely affected patients seen at a tertiary care center. Additionally, the 10-year study period encompassed changes in clinical practice and therapeutic approaches that may have influenced outcomes over time. The lack of long-term follow-up data prevents assessment of long-term maternal and child health outcomes.

The clinical implications of our findings are significant for healthcare providers caring for women with SLE. Preconception counseling should emphasize the importance of achieving disease remission, optimizing medications, and planning pregnancy timing. During pregnancy, close collaboration between rheumatology, maternal-fetal medicine, and other specialists is essential for optimal outcomes. Post-delivery care should include continued monitoring for disease flares and long-term follow-up of both mother and child.

Future research directions should include prospective studies with longer follow-up periods, investigation of novel biomarkers for predicting pregnancy complications, evaluation of emerging therapeutic options, and assessment of long-term outcomes in mothers and children. Additionally, development of standardized protocols for monitoring and management could help optimize care across different healthcare settings.

Conclusion

This comprehensive retrospective analysis demonstrates that while systemic lupus erythematosus significantly increases the risk of pregnancy complications, careful pre-conception planning, optimal disease management, and multidisciplinary care can substantially improve outcomes for both mothers and infants. The study confirms several key principles for managing SLE pregnancies: the critical importance of achieving disease remission before conception, the protective effects of hydroxychloroquine therapy, the particular challenges posed by lupus nephritis, and the need for specialized monitoring throughout pregnancy and the postpartum period.

The findings strongly support current recommendations for pre-conception counseling in all women with SLE of reproductive age, emphasizing disease optimization, medication adjustment, and risk assessment before pregnancy. The dramatic difference in outcomes between women with low versus high disease activity at conception underscores the importance of timing pregnancy during periods of disease quiescence whenever possible.

The protective effect of hydroxychloroquine therapy provides important guidance for medication management during pregnancy, supporting the continuation of this therapy throughout gestation in women with SLE. Conversely, the increased risks associated with lupus nephritis highlight the need for aggressive management of renal disease and consideration of pregnancy deferral until renal remission is achieved.

Healthcare providers caring for women with SLE should implement comprehensive pre-conception counseling

programs, establish multidisciplinary care teams, and develop standardized monitoring protocols to optimize pregnancy outcomes. The relatively low maternal mortality rate in our study, while encouraging, emphasizes the continued need for vigilant monitoring and prompt intervention when complications arise.

Future efforts should focus on developing predictive models for pregnancy complications, evaluating novel therapeutic approaches, and establishing evidence-based guidelines for monitoring and management. Additionally, research into long-term outcomes for both mothers and children will provide valuable insights into the extended implications of SLE pregnancies.

These findings contribute to the growing body of evidence supporting the feasibility of successful pregnancies in women with SLE when appropriate precautions are taken and optimal care is provided. With continued advances in understanding and management, the outlook for women with SLE desiring pregnancy continues to improve, offering hope for families affected by this challenging autoimmune condition.

References

- Tsokos GC. Systemic lupus erythematosus. N Engl J Med. 2011;365(22):2110-21.
- 2. Somers EC, Marder W, Cagnoli P, *et al.* Population-based incidence and prevalence of systemic lupus erythematosus: the Michigan Lupus Epidemiology and Surveillance program. Arthritis Rheumatol. 2014;66(2):369-78.
- 3. Rahman A, Isenberg DA. Systemic lupus erythematosus. N Engl J Med. 2008;358(9):929-39.
- 4. Buyon JP, Kim MY, Guerra MM, *et al.* Predictors of pregnancy outcomes in patients with lupus: a cohort study. Ann Intern Med. 2015;163(3):153-63.
- Clowse ME, Jameson M, Lin FC, Kao AH. A national study of the complications of lupus in pregnancy. Am J Obstet Gynecol. 2008;199(2):127.e1-6.
- 6. Andreoli L, Bertsias GK, Agmon-Levin N, *et al.* EULAR recommendations for women's health and the management of family planning, assisted reproduction, pregnancy and menopause in patients with systemic lupus erythematosus and/or antiphospholipid syndrome. Ann Rheum Dis. 2017;76(3):476-85.
- 7. Tektonidou MG, Andreoli L, Limper M, *et al.* EULAR recommendations for the management of antiphospholipid syndrome in adults. Ann Rheum Dis. 2019;78(10):1296-304.
- 8. Moroni G, Doria A, Giglio E, *et al*. Maternal outcome in pregnant women with lupus nephritis. A prospective multicenter study. J Autoimmun. 2016;74:194-200.
- 9. Imbasciati E, Tincani A, Gregorini G, *et al.* Pregnancy in women with pre-existing lupus nephritis: predictors of fetal and maternal outcome. Nephrol Dial Transplant. 2009;24(2):519-25.
- Miyakis S, Lockshin MD, Atsumi T, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). J Thromb Haemost. 2006;4(2):295-306.
- 11. Bramham K, Thomas M, Nelson-Piercy C, Khamashta M, Hunt BJ. First-trimester low-dose prednisolone in refractory antiphospholipid antibody-related pregnancy loss. Blood. 2011;117(25):6948-51.
- 12. Buyon JP, Hiebert R, Copel J, et al. Autoimmune-associated congenital heart block: demographics,

- mortality, morbidity, and recurrence rates obtained from a national neonatal lupus registry. J Am Coll Cardiol. 1998;31(7):1658-66.
- 13. Friedman DM, Kim MY, Copel JA, *et al.* Utility of cardiac monitoring in fetuses at risk for congenital heart block: the PR Interval and Dexamethasone Evaluation (PRIDE) prospective study. Circulation. 2008;117(4):485-93.
- 14. Flint J, Panchal S, Hurrell A, *et al.* BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding-Part I: standard and biologic disease modifying anti-rheumatic drugs and corticosteroids. Rheumatology (Oxford). 2016;55(9):1693-7.
- 15. Götestam Skorpen C, Hoeltzenbein M, Tincani A, *et al.* The EULAR points to consider for use of antirheumatic drugs before conception, and during pregnancy and lactation. Ann Rheum Dis. 2016;75(5):795-810.
- 16. Costedoat-Chalumeau N, Amoura Z, Duhaut P, *et al.* Safety of hydroxychloroquine in pregnant patients with connective tissue diseases: a study of one hundred thirty-three cases compared with a control group. Arthritis Rheum. 2003;48(11):3207-11.
- 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. 2017;79:17-27.
- Smyth A, Oliveira GH, Lahr BD, Bailey KR, Norby SM, Garovic VD. A systematic review and meta-analysis of pregnancy outcomes in patients with systemic lupus erythematosus and lupus nephritis. Clin J Am Soc Nephrol. 2010;5(11):2060-8.
- 19. Chakravarty EF, Nelson L, Krishnan E. Obstetric hospitalizations in the United States for women with systemic lupus erythematosus and rheumatoid arthritis. Arthritis Rheum. 2006;54(3):899-907.
- 20. Buyon JP, Kim MY, Guerra MM, *et al*. Kidney outcomes and risk factors for nephritis (flare/de novo) in a multiethnic cohort of pregnant patients with lupus. Clin J Am Soc Nephrol. 2017;12(6):940-6.
- 21. Aringer M, Costenbader K, Daikh D, et al. 2019 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Systemic Lupus Erythematosus. Arthritis Rheumatol. 2019;71(9):1400-12.
- 22. Gladman DD, Ibañez D, Urowitz MB. Systemic lupus erythematosus disease activity index 2000. J Rheumatol. 2002;29(2):288-91.
- 23. Lightstone L, Hladunewich MA. Lupus nephritis and pregnancy: concerns and controversies. Lupus. 2011;20(13):1469-79.
- 24. Soh MC, Kamp GA, Teng YKO, *et al.* Reproductive health in women with systemic lupus erythematosus. Semin Arthritis Rheum. 2020;50(4):577-87.