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THE COURSE OF PREGNANCY AND THE DEVELOPMENT OF OBSTETRIC COMPLICATIONS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Abstract

Systemic lupus erythematosus is a chronic autoimmune disease that predominantly affects women of reproductive age, making pregnancy management a major clinical concern. Pregnancy in patients with systemic lupus erythematosus is associated with an increased risk of maternal, fetal, and neonatal complications resulting from immune dysregulation, vascular involvement, and organ damage. Disease activity at conception, lupus nephritis, antiphospholipid syndrome, and cardiopulmonary involvement are among the principal factors contributing to adverse pregnancy outcomes. Maternal complications frequently include disease flares, hypertensive disorders, renal deterioration, and thromboembolic events, while fetal complications encompass pregnancy loss, intrauterine growth restriction, preterm delivery, and neonatal lupus manifestations. Evidence indicates that favorable pregnancy outcomes are more likely when conception occurs during periods of disease remission or stable low activity. Comprehensive preconception evaluation, individualized risk stratification, and close multidisciplinary monitoring throughout pregnancy and the postpartum period are essential for minimizing complications. An integrated clinical approach allows many women with systemic lupus erythematosus to

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achieve successful pregnancy outcomes despite the high-risk nature of the condition.

Keywords: Systemic lupus erythematosus; pregnancy; obstetric complications; lupus nephritis; antiphospholipid syndrome; maternal outcomes; fetal outcomes

Introduction

Systemic lupus erythematosus is a chronic, multisystem autoimmune disorder characterized by immune dysregulation and the production of a wide spectrum of autoantibodies, leading to heterogeneous clinical manifestations [1]. The disease course ranges from relatively mild forms to severe, life-threatening conditions, depending on the extent of organ involvement and disease activity. Clinically, SLE may affect the skin, musculoskeletal system, hematopoietic organs, serous membranes, kidneys, and central nervous system, manifesting as rash, arthritis, anemia, thrombocytopenia, serositis, nephritis, seizures, or psychosis. A defining feature of SLE is its relapsing–remitting nature, although a subset of patients demonstrates persistently active disease with progressive organ damage [2].

Epidemiological data indicate that SLE predominantly affects women, particularly those of reproductive age, which makes the interaction between SLE and pregnancy a major clinical concern. The incidence and prevalence of SLE show substantial variation according to sex and ethnicity. In population-based studies, the incidence in women is several times higher than in men, with the female-to-male ratio reaching its maximum in premenopausal age groups [3]. Ethnic disparities are also pronounced, with higher incidence and prevalence rates reported among women of African and Caribbean origin, while comparatively lower rates are observed in White, Asian, and certain other ethnic populations. Despite these variations, the global trend indicates an increasing number of women with SLE reaching childbearing age due to improvements in diagnostic approaches and long-term disease management [4].

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Advances in immunomodulatory therapy and multidisciplinary care have significantly improved survival rates in patients with SLE, resulting in a growing proportion of affected women considering pregnancy. However, pregnancy in the context of SLE remains a high-risk condition for both the mother and the fetus. The physiological immunological and hormonal changes of pregnancy may influence disease activity, while active SLE can adversely affect placental function and fetal development [5]. Maternal complications associated with SLE include disease flares, progression of renal involvement, development or worsening of hypertension, preeclampsia, and thromboembolic events. From the fetal perspective, SLE is associated with an increased risk of miscarriage, intrauterine growth restriction, preterm delivery, stillbirth, and neonatal lupus syndromes, including congenital heart block [6].

The relationship between pregnancy and the course of SLE is complex and remains a subject of ongoing debate. While some studies suggest that pregnancy does not necessarily exacerbate disease activity when conception occurs during periods of remission, others report a considerable incidence of flares, particularly in patients with active disease, lupus nephritis, or antiphospholipid antibodies. Conversely, the detrimental impact of SLE on pregnancy outcomes is more consistently documented, emphasizing the importance of careful risk stratification and individualized management [7].

Basic clinical considerations

Pregnancy in women with systemic lupus erythematosus is associated with an increased risk of both maternal and fetal–neonatal complications, reflecting the complex interaction between autoimmune disease activity and physiological changes of gestation. Maternal complications commonly include disease flares, progression of renal involvement, development or exacerbation of arterial hypertension, preeclampsia, and venous thromboembolic events. From the fetal and neonatal perspective, adverse outcomes may manifest as pregnancy loss,

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intrauterine growth restriction, preterm birth, and neonatal lupus syndromes, including congenital cardiac manifestations [8, 10].

Optimal pregnancy outcomes in patients with systemic lupus erythematosus are closely linked to a structured and coordinated multidisciplinary approach. Effective clinical care requires collaboration among specialists with expertise in autoimmune disease and high-risk obstetrics, including rheumatologists, obstetricians, nephrologists, fetal medicine specialists, cardiologists, neonatologists, and trained midwifery staff [11]. Such an approach facilitates comprehensive assessment of maternal disease status and timely identification of pregnancy-related risks.

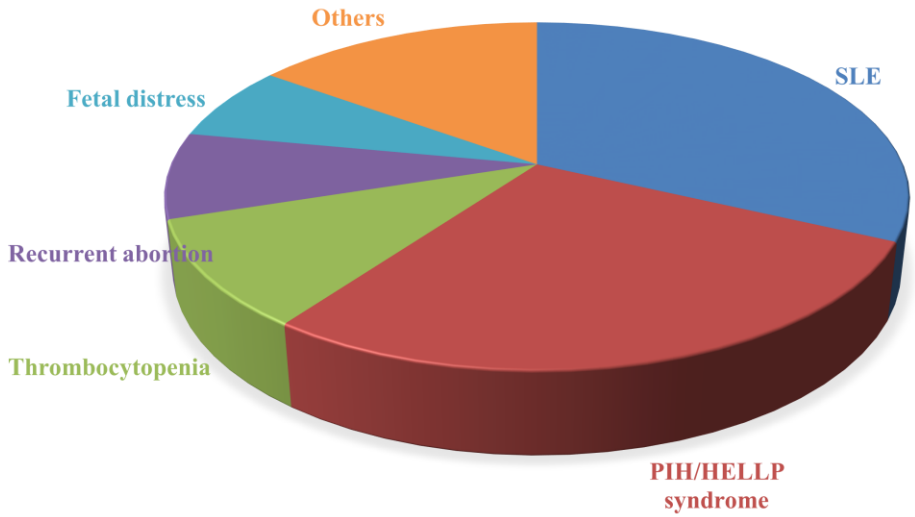

Figure 1. Major maternal indications for cesarean delivery in pregnancies complicated by systemic lupus erythematosus.

Preconception evaluation represents a critical component of clinical management and should involve thorough risk assessment, stratification based on disease activity and organ involvement, and individualized counseling tailored to each patient's clinical profile. Achieving stable disease control prior to conception

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significantly reduces the likelihood of adverse maternal and fetal outcomes. Once pregnancy is confirmed, early enrollment in specialized antenatal care is essential, with coordinated rheumatologic and obstetric follow-up initiated during the first trimester and continued throughout gestation [12].

Close surveillance during pregnancy allows for early detection and prompt management of disease flares and obstetric complications. Individualized antenatal management plans should be adapted dynamically in response to changes in disease activity or pregnancy course. Postpartum care is equally important, as the puerperium represents a period of increased vulnerability to disease exacerbation. Therefore, tailored postnatal management, including appropriate neonatal evaluation and continued rheumatologic follow-up, is necessary to ensure sustained maternal health and favorable long-term outcomes [13].

This clinical framework underscores the importance of integrated care across the preconception, antenatal, intrapartum, and postpartum periods in women with systemic lupus erythematosus, providing a foundation for minimizing complications and optimizing pregnancy outcomes.

Preconception risk assessment and stratification in systemic lupus erythematosus

Preconception consultation in women with systemic lupus erythematosus plays a pivotal role in identifying pregnancy-related risks and optimizing subsequent maternal and fetal outcomes. A comprehensive clinical assessment should be undertaken to define the individual risk profile prior to conception. This evaluation must incorporate a detailed analysis of past and current disease activity, including the timing, severity, and frequency of recent disease flares. Particular attention should be paid to the presence of irreversible organ damage, especially involving the cardiovascular, pulmonary, and renal systems, as these factors are strongly associated with adverse pregnancy outcomes.

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Table 1. Preconception consultation: comprehensive information gathering in women with systemic lupus erythematosus

Assessment domain	Key elements to be evaluated	Clinical relevance for pregnancy
Past and current disease activity	Disease duration; activity status; frequency and severity of flares; time since last flare	Active disease increases risk of maternal and fetal complications
Preexisting organ damage	Renal, cardiovascular, pulmonary, neurological involvement	Associated with preeclampsia, preterm birth, maternal morbidity
Serological profile	Anti-dsDNA; anti-Ro/SSA; anti-La/SSB; antiphospholipid antibodies; complement levels	Predicts pregnancy loss, placental dysfunction, neonatal lupus
Medication history	Current and prior immunosuppressive therapy; corticosteroids; teratogenic exposure	Optimization reduces disease flares and fetal risk
Additional medical disorders	Hypertension; diabetes; chronic kidney disease; venous thromboembolism history	Independently increases obstetric risk
Past obstetric history	Miscarriage; stillbirth; preterm birth; SGA; neonatal lupus	Previous adverse outcomes predict recurrence
Baseline clinical evaluation	Blood pressure; urinalysis	Early detection of renal and hypertensive disorders
Laboratory investigations	FBC; U&E; creatinine; liver function tests; serology	Establishes baseline disease and organ function
Organ-specific investigations	Echocardiography; pulmonary function tests; renal imaging if indicated	Assesses pregnancy tolerance of affected organs

A thorough review of current and previous pharmacological therapy is essential, with special emphasis on medications that may influence fertility, disease control, or fetal safety. In parallel, recent immunological and serological parameters should be assessed, including anti–double-stranded DNA antibodies, anti-Ro and anti-La antibodies, antiphospholipid antibodies, and complement levels, as these markers provide valuable prognostic information regarding disease activity and obstetric risk [14].

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The presence of coexisting medical conditions must be carefully documented, particularly arterial hypertension, diabetes mellitus, chronic kidney disease, and a history of venous thromboembolism, as these comorbidities further compound pregnancy-related risks. A detailed obstetric history is equally important and should include information on all previous pregnancies, gestational age at delivery, and pregnancy outcomes. Special consideration should be given to prior fetal or neonatal losses and complications, such as miscarriage, stillbirth, small-for-gestational-age neonates, preterm birth, congenital heart block, neonatal lupus manifestations, and maternal complications including preeclampsia or disease flares during the antenatal or postpartum periods [15].

Table 2. Relative contraindications to pregnancy in women with systemic lupus erythematosus

Clinical condition	Implications for pregnancy
Severe lupus flare (including renal flare) within the past 6 months	High risk of maternal deterioration and adverse fetal outcomes
Recent stroke (within the past 6 months)	Increased maternal morbidity and mortality during pregnancy
Pulmonary hypertension	Associated with extremely high maternal and perinatal mortality
Moderate-to-severe heart failure	Limited cardiovascular reserve and poor pregnancy tolerance
Severe valvular heart disease	High risk of cardiac decompensation during gestation
Severe restrictive lung disease	Impaired oxygenation and reduced maternal–fetal tolerance
Chronic kidney disease stage 4–5	High likelihood of renal deterioration, preeclampsia, and preterm birth
Uncontrolled arterial hypertension	Increased risk of stroke, placental insufficiency, and fetal growth restriction
Previous severe early-onset (<28 weeks) preeclampsia or HELLP syndrome despite aspirin and heparin therapy	High recurrence risk and poor maternal–fetal prognosis

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Baseline clinical evaluation should include measurement of blood pressure and urinalysis to identify preexisting hypertension or renal involvement [16]. Laboratory investigations should comprise a complete blood count, renal and hepatic function tests, and updated serological profiling when recent data are unavailable. In selected cases, additional organ-specific investigations, such as echocardiography or pulmonary function testing, may be required to accurately assess functional reserve in patients with known organ involvement.

Based on the comprehensive preconception assessment, women with systemic lupus erythematosus may be stratified according to disease status and pregnancy-related risk. This stratification enables individualized counseling and informed decision-making regarding pregnancy planning, timing of conception, and the intensity of monitoring required during gestation. Such an approach forms the foundation for reducing obstetric complications and improving overall pregnancy outcomes in this high-risk population.

Preconception counseling and individualized pregnancy planning in systemic lupus erythematosus

Risk stratification of women with systemic lupus erythematosus prior to pregnancy provides a rational framework for individualized clinical decision-making and counseling. Categorization based on disease activity, treatment stability, and the presence of organ damage allows clinicians to tailor recommendations according to each patient's specific clinical context rather than adopting a uniform approach [17].

Women with SLE in sustained remission or with stable low disease activity represent the most favorable group for pregnancy planning. In such cases, pharmacological therapy should be carefully reviewed and adjusted to ensure disease control while maintaining fetal safety. These patients can generally be advised that pregnancy may be planned, provided that close multidisciplinary monitoring is ensured.

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In contrast, women with recently diagnosed SLE or those with active disease require a more cautious approach. Pregnancy should be deferred until adequate disease control is achieved, and effective contraception should be encouraged during this period. Medical management should focus on optimizing immunosuppressive therapy using agents compatible with pregnancy, such as hydroxychloroquine and azathioprine. Regular clinical reassessment is essential, and pregnancy planning may be reconsidered once disease activity decreases or remission is attained.

Patients with severe organ dysfunction or established irreversible organ damage constitute a particularly high-risk group. In these circumstances, the potential maternal and fetal risks associated with pregnancy are substantial. Comprehensive counseling should therefore include a clear discussion of health-related risks, potential pregnancy complications, and unfavorable prognostic outcomes. In such cases, pregnancy is generally discouraged, and alternative pathways to parenthood, including adoption or surrogacy using own or donor oocytes, should be discussed in a supportive and informed manner.

Once disease stability has been achieved, preconception counseling should extend beyond disease control to encompass a detailed discussion of potential medical and obstetric risks. Although pregnancy in women with SLE is typically classified as high risk, individualized care strategies combined with vigilant multidisciplinary surveillance throughout pregnancy and the puerperium are associated with a high likelihood of successful outcomes.

The impact of pregnancy on maternal disease includes the risk of disease flares and progression of organ damage, whereas the influence of SLE on pregnancy primarily manifests as hypertensive disorders, thromboembolic events, and adverse fetal outcomes. Previous obstetric complications further increase the probability of recurrence in subsequent pregnancies and should be carefully integrated into risk assessment.

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Women with active disease at conception or within the preceding six months, lupus nephritis, or cardiac and pulmonary involvement are particularly susceptible to disease exacerbations and obstetric complications during pregnancy. Additionally, the presence of thrombotic or obstetric antiphospholipid syndrome confers a markedly increased risk of venous thromboembolism and pregnancy loss, often necessitating prophylactic therapy with low-dose aspirin and/or low-molecular-weight heparin. Patients with anti-Ro or anti-La antibodies require targeted counseling regarding the risk of fetal–neonatal complications, including congenital heart block and neonatal lupus syndromes [18].

A clear distinction between antiphospholipid antibody positivity and clinically defined antiphospholipid syndrome is essential during counseling, as management strategies and prognostic implications differ substantially. Incorporating these considerations into preconception counseling ensures informed decision-making and forms a critical component of comprehensive pregnancy planning in women with systemic lupus erythematosus.

Table 3. Factors affecting pregnancy outcomes in systemic lupus erythematosus

Factor	Description	Impact on pregnancy outcome
Disease activity	Presence of active or recently active systemic lupus erythematosus	Associated with increased risk of flares, preeclampsia, preterm birth, and fetal loss
Lupus nephritis	Renal involvement including hypertension and impaired renal function	Strong predictor of adverse maternal and fetal outcomes, including growth restriction
Anti-Ro/SSA and anti-La/SSB antibodies	Maternal autoantibodies crossing the placenta	Increased risk of congenital heart block and neonatal lupus
Antiphospholipid syndrome	Presence of antiphospholipid antibodies with clinical manifestations	Associated with pregnancy loss, placental insufficiency, and thromboembolic events
Cardiac and pulmonary involvement	Underlying heart or lung disease related to SLE	Reduced maternal physiological reserve and increased obstetric complications

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Antiphospholipid syndrome is diagnosed in the presence of antiphospholipid antibodies accompanied by clinically significant thrombotic or obstetric manifestations [19]. The thrombotic form of antiphospholipid syndrome is defined by one or more documented episodes of arterial, venous, or small-vessel thrombosis. In contrast, obstetric antiphospholipid syndrome is characterized by specific adverse pregnancy outcomes, including unexplained fetal death at or beyond ten weeks of gestation, preterm delivery of a morphologically normal fetus before thirty-four weeks due to hypertensive disorders of pregnancy or placental insufficiency, as well as recurrent early pregnancy loss, defined as three or more consecutive unexplained miscarriages before ten weeks of gestation.

Comparative analyses of pregnancy outcomes in women with isolated antiphospholipid antibody positivity and those with established obstetric antiphospholipid syndrome demonstrate clinically important differences. While low-dose aspirin therapy during pregnancy is commonly administered to both groups, women with obstetric antiphospholipid syndrome often require additional anticoagulation with low-molecular-weight heparin, particularly in the presence of previous thromboembolic events, severe pregnancy complications, or adverse outcomes despite aspirin therapy. Evidence indicates that women with isolated antiphospholipid antibodies generally experience pregnancy outcomes comparable to those observed in the general obstetric population. In contrast, obstetric antiphospholipid syndrome is associated with substantially increased rates of pregnancy-induced hypertension and preeclampsia, higher incidence of pregnancy loss, lower neonatal birthweight, and a greater frequency of small-for-gestational-age infants.

Beyond its obstetric implications, antiphospholipid antibody positivity should also be regarded as an independent risk factor for thromboembolic events during pregnancy and the postpartum period. The need for anticoagulant prophylaxis should therefore be guided by the cumulative thrombotic risk profile. In women with multiple additional risk factors, antenatal administration of low-molecular-

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weight heparin may be indicated, whereas in those with fewer risk factors, anticoagulation may be initiated later in pregnancy or limited to the postpartum period. Extended postpartum thromboprophylaxis is particularly important, as the puerperium represents a period of heightened thrombotic risk.

Women with thrombotic antiphospholipid syndrome, many of whom require long-term anticoagulant therapy, represent a high-risk subgroup. During pregnancy, these patients typically require intensified thromboprophylaxis with therapeutic or intermediate doses of low-molecular-weight heparin throughout gestation and for an extended period following delivery, until safe transition back to long-term oral anticoagulation is achieved. Management of such cases necessitates close collaboration between obstetricians, rheumatologists, and hematologists with expertise in high-risk pregnancy and autoimmune thrombophilia [20].

This risk-adapted approach to antiphospholipid antibody positivity and antiphospholipid syndrome underscores the importance of individualized assessment and targeted prophylactic strategies in improving maternal and fetal outcomes in pregnancies complicated by systemic lupus erythematosus.

Postpartum contraception and reproductive planning in systemic lupus erythematosus

The postpartum period represents a critical phase in the comprehensive management of women with systemic lupus erythematosus, requiring continued medical surveillance and appropriate reproductive counseling. In addition to routine rheumatologic and obstetric follow-up, postpartum care should include a structured clinical assessment, discussion of contraceptive options, and coordination of maternal and neonatal health evaluations. Effective counseling during this period is essential, as planned pregnancies in women with chronic autoimmune diseases are consistently associated with reduced complication rates and improved pregnancy outcomes.

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Contraceptive counseling should be individualized, taking into account disease activity, thrombotic risk, comorbid conditions, and patient preferences. Barrier methods, including male and female condoms, diaphragms, caps, and sponges, are widely accessible and provide protection against sexually transmitted infections. However, their relatively high failure rates with typical use limit their effectiveness as sole contraceptive strategies in women for whom unplanned pregnancy poses significant medical risk.

Hormonal contraceptive methods require careful risk assessment in patients with SLE. Estrogen-containing contraceptives are associated with an increased risk of venous thromboembolism and are therefore contraindicated in women with antiphospholipid antibodies or antiphospholipid syndrome, moderate-to-severe active disease, lupus nephritis, uncontrolled hypertension, obesity, smoking, or a prior history of thrombotic events. In contrast, women with stable or inactive disease and without significant thrombotic risk factors may be considered suitable candidates for combined oral contraceptives, as evidence suggests that their use does not increase disease flares or exacerbate disease activity in this subgroup.

Progestogen-only contraceptive methods, including oral formulations, subdermal implants, injectable preparations, and levonorgestrel-releasing intrauterine systems, represent safe and effective alternatives for many women with SLE. These methods are particularly advantageous in patients with contraindications to estrogen, as they do not increase thromboembolic risk. Long-acting reversible contraceptives offer high efficacy, reduced dependence on user compliance, and prolonged duration of action. In addition, intrauterine systems may confer non-contraceptive benefits, such as reduction in menstrual blood loss, which can be advantageous in women with anemia or on anticoagulant therapy.

Non-hormonal intrauterine devices, including copper-containing coils, provide highly effective contraception without systemic hormonal exposure and do not increase thrombotic risk. However, their potential to increase menstrual bleeding should be considered, particularly in women receiving long-term anticoagulation.

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Conclusion

Pregnancy in women with systemic lupus erythematosus remains a clinically challenging condition due to the complex interplay between autoimmune disease activity and the physiological adaptations of gestation. The available evidence indicates that SLE is associated with a higher risk of maternal complications, including disease flares, hypertensive disorders, renal impairment, and thromboembolic events, as well as adverse fetal and neonatal outcomes such as pregnancy loss, intrauterine growth restriction, preterm birth, and neonatal lupus syndromes. Disease activity at conception, the presence of lupus nephritis, antiphospholipid syndrome, and cardiac or pulmonary involvement represent key determinants of unfavorable pregnancy outcomes, underscoring the importance of comprehensive risk assessment and stratification.

Optimizing pregnancy outcomes in this high-risk population requires an integrated, multidisciplinary approach spanning the preconception, antenatal, intrapartum, and postpartum periods. Effective preconception counseling, achievement of disease remission or stable low activity prior to conception, individualized antenatal management, and appropriate postpartum follow-up, including contraceptive planning, are central to reducing complications and improving maternal and fetal prognosis. With careful planning, close surveillance, and coordinated care involving rheumatology, obstetrics, and related specialties, successful pregnancy outcomes are achievable for many women with systemic lupus erythematosus, reinforcing the value of personalized and evidence-based management strategies.

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