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Elevated Preeclampsia Risk in Pregnant Patients with Systemic Lupus Erythematosus: A Multidisciplinary Review

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Purpose

Navigating the complexities of distinguishing between pregnancy-associated symptoms and those linked to systemic lupus erythematosus (SLE) presents a formidable task. The involvement of various specialties such as obstetrics, rheumatology, nephrology, and primary care is essential for comprehensive patient care. Specifically, the challenge of discerning between preeclampsia and an SLE flare is considerable, given the overlapping clinical features. Distinguishing preeclampsia in the context of SLE requires a nuanced understanding of both conditions' pathophysiology. Understanding why there is an increased risk is crucial for practitioners to effectively manage preeclampsia in patients with SLE. The incidence of preeclampsia is significantly higher in patients with SLE, emphasizing the importance of tailored care and vigilant monitoring throughout pregnancy.

This review aims to identify the underlying explanation for the increased risk of preeclampsia in patients with systemic lupus erythematosus. Additionally, the study seeks to consolidate and assess current insights into the pathogenesis, symptoms, and management of preeclampsia in patients with SLE, advocating for a multidisciplinary treatment approach.

Methods

The study was executed by investigating the following databases: PubMed, National Institutes of Health, Science Direct, Biomed Central, and Scopus. Inclusion criteria consisted of studies in reference to preeclampsia as an adverse pregnancy outcome (APO) in patients with SLE conducted between 1999 and present. Studies in non-English languages and those that were not open access were excluded. Articles were screened and read to determine relevance to our inquiry of the pathophysiology of the increased risk of preeclampsia in patients with SLE.

Salmon	• Genetic variants in complement proteins membrane cofactor protein (MCP) and complement factor I (CHI) • Complement system activation dysregulation
Andrade	• ↑ IFNa-1 • sFlt1 sensitization

Figure 1: Results from analyses of the PROMISSE study

Tanner	• Women with comorbidities may develop preeclampsia with a milder elevation in sFLT-1: PIGF than do women without comorbidities
Mayer-Pickel	• 9% of the women with SLE developed early-onset preeclampsia and they had a significantly higher sFLT-1:PIGF ratio and endoglin levels compared to those who did not
Leanos-Miranda	• Changes in levels of sFLT-1, PIGF and endoglin (sEng) varied between SLE patients that developed early-onset and late-onset preeclampsia.

Figure 2: Studies with main findings regarding sFlt-1

Xue	• Identified ten immunophenotypes significantly associated with increased PE risk • Pregnant women with PE had higher concentrations of FGF-21 but lower concentrations of IL-10 and Caspase-8 compared to normotensive pregnant women
Chighizola	• Hypocomplementemia during gestation can predict poor outcomes in SLE pregnancies, with markedly decreased levels of C1q and C4 in early and late-onset preeclampsia
Hong	• Pregnant lupus patients with fetal complications had higher interferon, plasma cell, and activated CD4+ T cell counts. • In preeclampsia, persistent upregulation of the neutrophil signature was identifiable early (<15 weeks), corresponding to increased immature neutrophils.
Canti	• Late pregnancy complications, such as preeclampsia, were more likely in patients who were positive for antiphosphatidylserine/prothrombin antibodies (aPS/PT)

Figure 3: Additional studies suggesting the pathophysiology behind increased risk of preeclampsia with SLE

Results

We identified 9 studies fitting our inclusion criteria. Three studies exhibited a theme of heightened sFLT-1:PIGF ratios and showcased a stratified approach to predicting early and late onset preeclampsia. Two studies displayed an association of increased INFa with preeclampsia development. Dysregulation of the complement system was a common finding in two studies. Additional findings include antiphosphatidylserine/prothrombin antibodies association, as well as certain immunophenotypes.

Conclusions

This review highlights the complex interplay between SLE and the heightened risk of preeclampsia in pregnant patients. The identified studies emphasize key pathogenic mechanisms, including elevated sFLT-1 ratios, increased INFa levels, complement system dysregulation, and specific immunophenotypic markers. These findings advance our understanding of pathophysiology, but also necessitate a multidisciplinary approach to effectively manage and mitigate the risks associated with preeclampsia in this population. Continued research and collaboration among specialties are imperative to refine diagnostic criteria and therapies, ultimately enhancing care for pregnant patients with SLE.

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