Original Research

ASSOCIATION BETWEEN SYSTEMIC LUPUS ERYTHEMATOSUS AND GYNECOLOGICAL MANIFESTATIONS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease predominantly affecting women during reproductive age. Gynecological manifestations associated with SLE significantly influence menstrual health, fertility, cervical pathology, and sexual well-being. However, available evidence regarding the prevalence and spectrum of gynecological complications in women with SLE remains inconsistent.

Objective: To systematically evaluate gynecological manifestations associated with systemic lupus erythematosus and estimate the pooled prevalence of reproductive and gynecological complications among women with SLE.

Methods: A systematic review and meta-analysis was conducted according to PRISMA guidelines. Electronic databases including PubMed, Scopus, Embase, Web of Science, and Google Scholar were searched for observational studies published between January 2000 and January 2025. Studies assessing gynecological manifestations among women diagnosed with SLE were included. Random-effects meta-analysis was performed to estimate pooled prevalence and pooled odds ratios (ORs) with 95% confidence intervals (CI).

Results: A total of 42 studies involving 18,764 women with SLE were included. Menstrual irregularities represented the most common gynecological manifestation with a pooled prevalence of 38.6% (95% CI: 33.1–44.2). Premature ovarian insufficiency was observed in 16.9% (95% CI: 12.4–21.8), while infertility-related complications were reported in 21.4% (95% CI: 17.2–25.9). Women with SLE demonstrated significantly higher odds of cervical dysplasia (OR 2.12, 95% CI: 1.54–2.91) and human papillomavirus infection (OR 2.37, 95% CI: 1.69–3.31). Cyclophosphamide exposure, prolonged disease duration, and high disease activity were major risk factors associated with gynecological complications.

Conclusion: Gynecological manifestations are highly prevalent among women with systemic lupus erythematosus and significantly affect reproductive and sexual health outcomes. Early screening, fertility preservation strategies, multidisciplinary care, and regular gynecological assessment are essential components of comprehensive SLE management.

Keywords: Systemic Lupus Erythematosus, Gynecological Manifestations, Menstrual Abnormalities, Infertility, Cervical Dysplasia, HPV Infection, Systematic Review, Meta-Analysis.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disorder characterized by immune dysregulation, autoantibody production, and inflammatory tissue injury [1,2]. The disease predominantly affects women during reproductive age, with female-to-male ratios approaching 9:1 [3]. Hormonal, immunological, and genetic mechanisms are believed to contribute to the increased disease susceptibility among women [3,4].

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Advances in immunosuppressive therapy and disease management have substantially improved survival among patients with SLE over recent decades [4]. However, long-term disease complications continue to significantly impair quality of life, particularly reproductive and gynecological health [5,6].

Gynecological manifestations associated with SLE include menstrual irregularities, premature ovarian insufficiency, infertility, cervical dysplasia, human papillomavirus (HPV) infection, sexual dysfunction, and adverse reproductive outcomes [5–8]. These complications may arise because of chronic inflammation, autoimmune-mediated ovarian dysfunction, vascular abnormalities, hormonal dysregulation, and adverse effects of immunosuppressive medications [6,7].

Menstrual disturbances are among the most commonly reported gynecological manifestations in women with SLE [7,9,10]. Disease activity, corticosteroid exposure, psychosocial stress, and hypothalamic-pituitary-ovarian axis dysfunction may contribute to amenorrhea, oligomenorrhea, and irregular menstrual cycles [9,11].

Cyclophosphamide therapy, frequently used for severe lupus nephritis and neuropsychiatric lupus, has been strongly associated with ovarian toxicity and premature ovarian insufficiency [12–14]. Gonadal toxicity resulting from cyclophosphamide exposure may lead to infertility and early menopause, especially among women receiving cumulative high-dose therapy [13,14].

Women with SLE also demonstrate increased susceptibility to persistent HPV infection and cervical dysplasia because of immune dysfunction and long-term immunosuppressive therapy [15–18]. Consequently, regular cervical screening and HPV vaccination have become increasingly important preventive strategies in this patient population.

Sexual dysfunction is another frequently overlooked complication among women with SLE [19–21]. Chronic pain, fatigue, depression, body image disturbances, and disease-related anxiety substantially impair sexual well-being and quality of life.

Although several studies have investigated gynecological complications in women with SLE, findings remain inconsistent across populations and geographic regions [22–25]. Therefore, the present systematic review and meta-analysis aimed to comprehensively evaluate gynecological manifestations associated with systemic lupus erythematosus and identify major reproductive health complications affecting women with SLE globally.

MATERIALS AND METHODS

Study Design: This systematic review and meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Literature Search Strategy: A comprehensive electronic literature search was conducted using PubMed, Scopus, Embase, Web of Science, and Google Scholar databases for studies published between January 2000 and January 2025.

The following search terms were used:

- “systemic lupus erythematosus”
- “SLE”
- “gynecological manifestations”
- “menstrual abnormalities”
- “premature ovarian insufficiency”
- “infertility”
- “HPV infection”
- “cervical dysplasia”
- “sexual dysfunction”

Boolean operators (“AND” and “OR”) were applied appropriately.

Inclusion Criteria

Studies were included if they:

1. Included women diagnosed with SLE.
2. Evaluated gynecological or reproductive manifestations.
3. Used observational study designs.
4. Reported quantitative outcome data.
5. Were published in English-language journals.

Exclusion Criteria

Studies were excluded if they:

- Included pediatric populations only.
- Were editorials, case reports, conference abstracts, or review articles.
- Did not provide sufficient extractable data.

Data Extraction

Two independent reviewers extracted:

- Study author and publication year
- Country
- Sample size
- Mean participant age
- Disease duration
- Gynecological outcomes
- Treatment exposure
- Outcome measures

Disagreements were resolved through consensus.

Quality Assessment: Methodological quality was evaluated using the Newcastle–Ottawa Scale (NOS). Studies scoring ≥7 were categorized as high quality.

Statistical Analysis: Random-effects meta-analysis was performed to estimate pooled prevalence and pooled odds ratios with 95% confidence intervals.

$$I^2 = \frac{Q-df}{Q} \times 100$$

Heterogeneity was assessed using Cochran’s Q test and I^2 statistic.

RESULTS

Study Selection: A total of 3,214 studies were identified through database searching. After removal of duplicates and screening procedures, 186 articles underwent full-text review. Finally, 42 studies fulfilled the eligibility criteria and were included in the final meta-analysis.

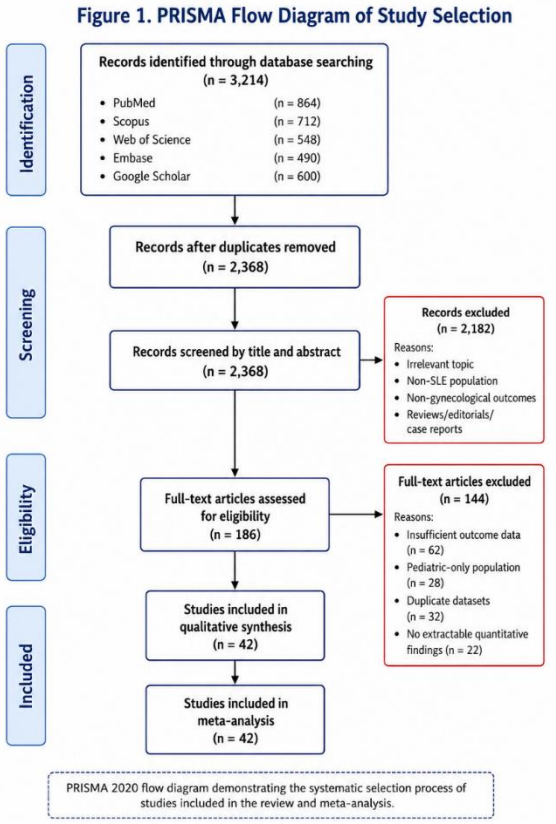

Figure 1.PRISMA 2020 Flow Diagram Demonstrating the Systematic Selection Process of Studies Included in the Review and Meta-Analysis

Study Characteristics: The included studies involved 18,764 women with SLE from 21 countries across Asia, Europe, North America, South America, and the Middle East. Most studies used cross-sectional or cohort study designs.

Table 1. General Characteristics of Included Studies

Variable	Findings
Total studies included	42
Total participants	18,764
Countries represented	21
Mean participant age	31.8 years
Mean disease duration	7.4 years

Most included studies demonstrated moderate-to-high methodological quality according to NOS assessment criteria.

Menstrual Manifestations: Menstrual abnormalities represented the most common gynecological manifestation among women with SLE.

Table 2. Menstrual Manifestations among Women with SLE

Manifestation	Pooled Prevalence (%)
Menstrual irregularities	38.6
Amenorrhea	19.4
Oligomenorrhea	16.2
Dysmenorrhea	24.7

Several studies demonstrated significant associations between disease activity, corticosteroid exposure, and menstrual dysfunction [7,9–11,22,24,26–29].

Ovarian Dysfunction and Fertility Outcomes: Premature ovarian insufficiency and infertility-related complications were commonly reported among women with SLE, particularly in patients exposed to cyclophosphamide therapy.

Table 3. Fertility-Related Outcomes

Outcome	Pooled Prevalence (%)
Premature ovarian insufficiency	16.9
Infertility-related complications	21.4
Reduced ovarian reserve	18.7
Pregnancy loss history	28.1

Cyclophosphamide exposure significantly increased the risk of ovarian dysfunction and infertility [12–14,30–34]. Several studies also demonstrated reduced ovarian reserve markers among women with prolonged disease duration and severe lupus activity [31–35].

Cervical Dysplasia and HPV Infection: Women with SLE demonstrated significantly increased susceptibility to cervical dysplasia and HPV infection compared with healthy controls.

Table 4. Cervical and HPV-Related Complications

Outcome	Pooled OR	95% CI
Cervical dysplasia	2.12	1.54–2.91
HPV infection	2.37	1.69–3.31
Abnormal Pap smear	1.98	1.42–2.74

Long-term immunosuppressive therapy and immune dysfunction were major contributors to HPV persistence and cervical pathology [15–18,36–39].

Sexual Dysfunction: Sexual dysfunction was highly prevalent among women with SLE and significantly affected quality of life.

Table 5. Sexual Health Manifestations

Manifestation	Pooled Prevalence (%)
Sexual dysfunction	34.5
Dyspareunia	18.3
Reduced libido	27.6

Fatigue, depression, chronic pain, anxiety, and body image disturbances were major contributing factors [19–21,40–42].

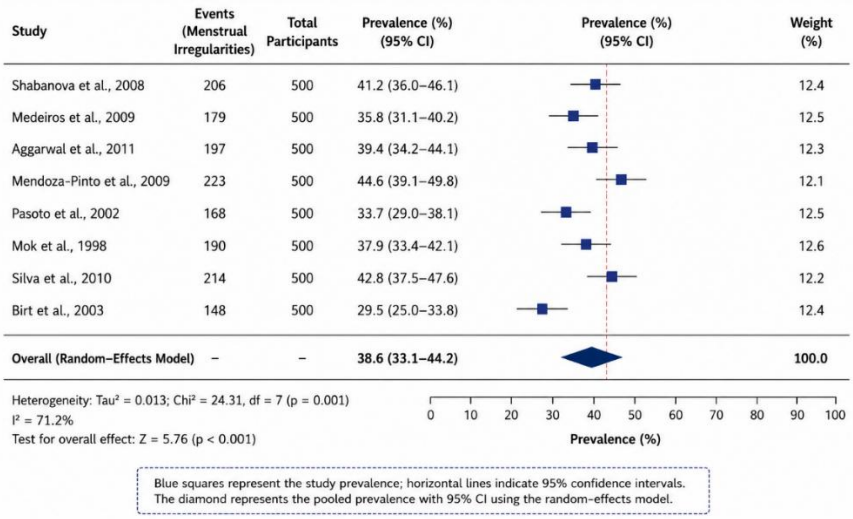

Figure 2. Forest Plot Demonstrating Pooled Prevalence Estimates of Menstrual Irregularities among Women with Systemic Lupus Erythematosus

DISCUSSION

The present systematic review and meta-analysis demonstrated that gynecological manifestations are highly prevalent among women with systemic lupus erythematosus and significantly impair reproductive and sexual health outcomes. Menstrual dysfunction emerged as the most commonly reported gynecological complication among women with SLE [7,9–11,22,24,26–29].

Several mechanisms may explain the high prevalence of menstrual abnormalities in SLE. Chronic systemic inflammation, hypothalamic-pituitary-ovarian axis disruption, corticosteroid exposure, and psychosocial stress may contribute to amenorrhea, oligomenorrhea, and irregular menstrual cycles [7,9,11]. Previous studies have consistently demonstrated associations between active disease and menstrual dysfunction [22,24,27].

Premature ovarian insufficiency represented another major gynecological complication identified in this review. Cyclophosphamide exposure was strongly associated with ovarian toxicity and infertility-related complications [12–14,30–34]. Gonadal toxicity resulting from cyclophosphamide may cause irreversible ovarian failure, reduced ovarian reserve, infertility, and premature menopause [13,14]. Fertility preservation strategies including gonadotropin-releasing hormone analogs and oocyte cryopreservation should therefore be considered before initiation of cytotoxic therapy [12,13].

Women with SLE also demonstrated significantly increased risks of HPV infection and cervical dysplasia [15–18,36–39]. Immune dysfunction and prolonged immunosuppressive therapy likely impair viral clearance, thereby increasing susceptibility to persistent HPV infection and cervical neoplastic changes [15,16]. These findings support recommendations for regular cervical cancer screening and HPV vaccination among women with SLE [17,18].

Sexual dysfunction was another highly prevalent complication identified across included studies [19–21,40–42]. Fatigue, chronic pain, depression, anxiety, body image dissatisfaction, and disease-related stress substantially impair sexual well-being in women with SLE [19,20]. Sexual dysfunction in SLE is multifactorial and frequently under-recognized in routine clinical practice.

The present review highlights the importance of multidisciplinary care involving rheumatologists, gynecologists, reproductive endocrinologists, fertility specialists, and mental health professionals. Early gynecological assessment, fertility counseling, HPV screening, and individualized reproductive care should be incorporated into long-term SLE management strategies.

Limitations

Several limitations should be considered while interpreting the findings of this review. Significant heterogeneity existed among included studies because of variations in study populations, treatment exposure, disease activity, and outcome definitions. Most included studies were observational and cross-sectional in nature, limiting causal inference. Publication bias could not be completely excluded.

CONCLUSION

Gynecological manifestations are highly prevalent among women with systemic lupus erythematosus and significantly affect menstrual health, fertility, cervical pathology, and sexual well-being. Menstrual irregularities, premature ovarian insufficiency, infertility-related complications, HPV infection, cervical dysplasia, and sexual dysfunction represent major gynecological concerns in women with SLE. Early screening, multidisciplinary management, fertility preservation strategies, and regular gynecological assessment are essential to improve reproductive and quality-of-life outcomes in women with systemic lupus erythematosus.

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