ChinaRxiv

AI translation · View original & related papers at
chinarxiv.org/items/chinaxiv-201712.00228

Pregnancy Outcomes in 66 Patients with Systemic Lupus Erythematosus (Postprint)

Authors: Song Xiuzhen, Chen Jiamian, Zhou Qiugen

Date: 2017-12-21T00:00:00+00:00

Abstract

Objective: To investigate pregnancy outcomes and associated risk factors in patients with systemic lupus erythematosus (SLE). Methods: A retrospective analysis was conducted on clinical data of hospitalized pregnant SLE patients at Nanfang Hospital from October 2006 to September 2015, comparing pregnancy outcomes and maternal-fetal complications between the disease remission-mild activity group (SLEDAI 9) and the moderate-severe activity group (SLEDAI > 9), and analyzing risk factors for adverse pregnancy outcomes. Results: Sixty-six SLE patients had a total of 69 pregnancies, with an average age at SLE diagnosis of 22.9 ± 5.1 years; the average duration of SLE at pregnancy was 4.1 ± 3.6 years; during pregnancy, 45 cases (65.2%) received drug therapy, 44 cases (63.8%) received glucocorticoids, of which 27 cases (39.1%) received a dose less than 20 mg/d and 17 cases (24.6%) received a dose higher than 20 mg/d, 19 cases (27.5%) received hydroxychloroquine, and the average highest SLEDAI score during pregnancy was 6.8 ± 7.4. Compared with the remission-mild activity group, the moderate-severe activity group had a higher fetal loss rate [12 (54.5%) vs 12 (25.5%)] and lower neonatal birth weight [(2073.0 ± 778.7) g vs (2817.8 ± 533.7) g] ($P < 0.05$); the moderate-severe activity group had higher rates of new-onset SLE [9 (40.9%) vs 6 (12.8%)], hypertension [12 (54.5%) vs 3 (6.4%)], active lupus nephritis [22 (100%) vs 4 (8.5%)], pulmonary infection [5 (22.7%) vs 2 (4.3%)], and renal insufficiency [8 (36.4%) vs 2 (4.3%)] than the remission-mild activity group, with statistically significant differences ($P < 0.05$); active lupus nephritis (OR = 6.10, 95% CI: 1.43–25.96) was an independent risk factor for adverse pregnancy outcomes. Conclusion: Moderate-to-severe lupus activity during pregnancy in SLE patients increases fetal loss and maternal complications, and active lupus nephritis is an independent risk factor for adverse pregnancy outcomes. Pregnancy outcomes in lupus patients still need further improvement; during pregnancy, various indicators of SLE patients should be regularly monitored, medication should be used rationally, and lupus activity should be controlled to achieve favorable pregnancy outcomes.

Full Text

Abstract: Objective

To investigate pregnancy outcomes and associated risk factors in women with systemic lupus erythematosus (SLE).

Methods

We conducted a retrospective analysis of clinical data from SLE patients with pregnancies admitted to Nanfang Hospital between October 2006 and September 2015. Patients were stratified into remission-mild activity (SLEDAI 9) and moderate-severe activity (SLEDAI >9) groups to compare pregnancy outcomes and maternal-fetal complications, and to identify risk factors for adverse pregnancy outcomes.

Results

Sixty-six SLE patients with 69 pregnancies were included. Mean age at SLE diagnosis was 22.9±5.1 years, and mean disease duration before pregnancy was 4.1±3.6 years. During pregnancy, 45 patients (65.2%) received pharmacological treatment, including 44 (63.8%) treated with glucocorticoids (27 at <20 mg/d and 17 at >20 mg/d) and 19 (27.5%) treated with hydroxychloroquine. Mean peak SLEDAI score during pregnancy was 6.8±7.4. Compared with the remission-mild activity group, the moderate-severe activity group exhibited a significantly higher fetal loss rate (12 [54.5%] vs 12 [25.5%]) and lower neonatal birth weight (2073.0±778.7 g vs 2817.8±533.7 g, P<0.05). The moderate-severe activity group also had significantly higher rates of new-onset SLE (9 [40.9%] vs 6 [12.8%]), hypertension (12 [54.5%] vs 3 [6.4%]), active lupus nephritis (22 [100%] vs 4 [8.5%]), pulmonary infection (5 [22.7%] vs 2 [4.3%]), and renal insufficiency (8 [36.4%] vs 2 [4.3%]) (P<0.05). Multivariate analysis identified active lupus nephritis as an independent risk factor for adverse pregnancy outcomes (OR=6.10, 95% CI: 1.43-25.96).

Conclusion

Moderate-to-severe SLE activity during pregnancy increases the risk of fetal loss and maternal complications. Active lupus nephritis is an independent risk factor for adverse pregnancy outcomes. Pregnancy outcomes in SLE patients require further improvement through regular monitoring, rational medication use, and optimal disease control to achieve favorable maternal-fetal outcomes.

Key words: systemic lupus erythematosus; pregnancy; adverse pregnancy outcomes

Introduction

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease that predominantly affects women of reproductive age. Historically, pregnancy in SLE patients was associated with numerous complications causing significant maternal and fetal morbidity, and these patients were generally advised against conception. However, advances in SLE management have enabled many patients to achieve sustained disease control, making pregnancy a viable consideration. Recent international studies have examined disease progression during pregnancy and its impact on maternal and fetal health, demonstrating improved outcomes compared with historical data [1-3]. Nevertheless, SLE flares occur in 23.3%–33% of pregnancies [4-6], and lupus nephritis recurs in 16.6%–30% of cases [4,7-8]. Compared with the general population, pregnant women with SLE face higher risks of mortality, preeclampsia, and preterm delivery [9-10], yet standardized treatment protocols remain lacking. Domestic research on this topic is limited and typically involves small sample sizes. Therefore, this study investigated pregnancy outcomes in SLE patients at our institution over the past decade and analyzed risk factors for adverse outcomes to provide clinical insights for improving maternal-fetal results.

Methods

Patient Selection

We identified 93 SLE patients with 102 pregnancies at Nanfang Hospital between October 2006 and September 2015. After excluding 33 patients due to incomplete clinical data, 69 pregnancies in 66 SLE patients were included in the final analysis [Figure 1: see original paper]. Collected data included demographic characteristics, obstetric history, SLE disease history, clinical manifestations during pregnancy, laboratory findings, medications used during pregnancy, pregnancy outcomes, and maternal-fetal complications.

Diagnostic Criteria and Disease Activity Assessment

All patients fulfilled the 1997 American College of Rheumatology revised criteria for SLE. Disease activity was assessed using the SLE Disease Activity Index (SLEDAI) developed by the University of Toronto [11]. SLEDAI scores <5 indicated inactive disease; scores of 5–9 indicated mild activity; 10–14 indicated moderate activity; and 15 indicated severe activity. Active lupus nephritis was defined as persistent proteinuria (>0.5 g/d or +++) or urinary casts (red blood cell, granular, or mixed), with or without elevated serum creatinine. Renal insufficiency was defined as serum creatinine 123.76 μmol/L, or an absolute increase of 26.4 μmol/L within 48 hours, or a 50% increase from baseline, or urine output <0.5 mL/(kg · h). Hypertension was defined as systolic blood pressure 140 mmHg and/or diastolic blood pressure 90 mmHg on three consecutive measurements, or the use of antihypertensive medication. Adverse pregnancy outcomes included fetal loss (miscarriage or stillbirth), preterm delivery, low birth weight

infants, or intrauterine growth restriction (IUGR).

Study Design

We employed a retrospective design to analyze the clinical characteristics of SLE patients. Based on the highest SLEDAI score during pregnancy, patients were stratified into remission-mild activity (SLEDAI 9) and moderate-severe activity (SLEDAI >9) groups. We compared fetal outcomes and maternal-fetal complications between groups and analyzed risk factors for adverse pregnancy outcomes.

Statistical Analysis

Statistical analysis was performed using SPSS 19.0 software. Continuous variables were expressed as mean ± standard deviation or median with range, and categorical variables as frequencies. Continuous data were compared using t-tests, while categorical data were analyzed using chi-square tests or Fisher' s exact test. Risk factors were evaluated using logistic regression analysis with entry criteria =0.05 and removal criteria =0.01. Statistical significance was set at P<0.05.

Results

Clinical Characteristics

The study included 69 pregnancies in 66 SLE patients. Mean age at SLE diagnosis was 22.9±5.1 years, and mean age at first pregnancy after diagnosis was 26.4±3.9 years. Mean disease duration at conception was 4.1±3.6 years. Patients required a mean of 1.2±0.5 hospital admissions during pregnancy. Mean peak SLEDAI score during pregnancy was 6.8±7.4, with 38 patients (55.1%) in the inactive group, 9 (13.0%) with mild activity, 9 (13.0%) with moderate activity, and 13 (18.8%) with severe activity. Mean SLEDAI score at delivery was 6.4±7.0. During pregnancy, 45 patients (65.2%) received pharmacological treatment, including 44 (63.8%) treated with glucocorticoids (27 at <20 mg/d and 17 at >20 mg/d). Hydroxychloroquine was used in 19 patients (27.5%), azathioprine in 2 (2.9%), and cyclosporine in 2 (2.9%); the latter three medications were used in patients with moderate-to-severe disease activity, always in combination with glucocorticoids and hydroxychloroquine. A history of lupus nephritis was present in 27 patients (39.1%), and 18 (26.1%) had undergone renal biopsy. During pregnancy, 15 patients (21.7%) developed hypertension, 17 (24.6%) had thrombocytopenia, mean complement C3 level was 0.82±0.36 g/L, and median serum creatinine was 47.0 (range 21.0–407.5) μmol/L.

Fetal Outcomes and Complications

After excluding 2 cases of unplanned pregnancy and 1 case of elective abortion due to maternal condyloma acuminata, there were 24 fetal losses (34.8%), in-

cluding 18 therapeutic abortions (26.1%), 3 stillbirths (4.3%), 2 spontaneous abortions (2.9%), and 1 maternal-fetal death (1.4%). Most fetal losses occurred in the second trimester (17 cases, 24.6%). Forty-two live births were delivered (60.9% of pregnancies), with mean birth weight 2640.5±672.0 g and mean gestational age 37.0±2.6 weeks. Full-term delivery occurred in 27 cases (39.1%), low birth weight infants in 15 (21.7%), preterm delivery in 15 (21.7%), IUGR in 6 (8.7%), and Apgar score <7 at 1 minute in 7 (10.1%) .

When stratified by SLE activity, the moderate-severe activity group demonstrated significantly higher fetal loss rates and lower rates of full-term delivery and neonatal birth weight compared with the remission-mild activity group .

Maternal Complications

New-onset SLE occurred in 15 patients (21.7%) during pregnancy, with 9 (60%) developing lupus nephritis—8 (53.3%) in the first trimester and 7 (46.7%) in the second trimester. Other maternal complications included hypertension in 15 (21.7%), active lupus nephritis in 26 (37.7%), gestational diabetes in 7 (10.1%), pulmonary infection in 7 (10.1%), preeclampsia/eclampsia in 7 (10.1%), renal insufficiency in 10 (14.5%), HELLP syndrome in 1 (1.4%), and maternal death in 1 (1.4%). The deceased patient had a history of multiple SLE flares and a previous therapeutic abortion in the third trimester due to disease exacerbation; during the index pregnancy, she discontinued medications spontaneously, experienced disease flare at 13 weeks, and died from heart failure at 16 weeks.

The moderate-severe activity group had significantly higher rates of new-onset SLE, hypertension, active lupus nephritis, pulmonary infection, and renal insufficiency compared with the remission-mild activity group ($P<0.05$) .

Risk Factor Analysis for Adverse Pregnancy Outcomes

Given the relatively high incidence of fetal loss, preterm delivery, low birth weight, and IUGR, and considering the limited case numbers, we combined these outcomes into a composite endpoint of adverse pregnancy outcomes for risk factor analysis. Univariate logistic regression identified hypertension, active lupus nephritis, and thrombocytopenia as risk factors, while pharmacological treatment during pregnancy was protective ($P<0.05$). Multivariate logistic regression confirmed active lupus nephritis as an independent risk factor for adverse pregnancy outcomes (OR=6.10, P=0.014) .

Discussion

This retrospective study of SLE pregnancies found that among 69 pregnancies, 42 live births were delivered (60.9%), with 15 (21.7%) resulting in preterm delivery. Maternal complications included hypertension in 15 (21.7%) and active lupus nephritis in 26 (37.7%), underscoring the persistent risks of pregnancy in SLE patients.

Reported fetal loss rates in international literature range widely from 4.6% to 34.0% [6,12-13], likely reflecting differences in disease severity among study populations. Domestic retrospective studies report fetal loss rates of 28.6%–31% [14-15], while our study found a rate of 34.8%. Preterm delivery rates of 20.8%–31% [9,13-14], low birth weight rates of 14.9%–32% [14-16], and IUGR rates of 5.6%–18.5% [9,12,14] have been reported internationally; our corresponding rates were 21.7%, 21.7%, and 8.7%, respectively, confirming suboptimal fetal outcomes in SLE pregnancies. Our composite analysis of adverse pregnancy outcomes (fetal loss, preterm delivery, low birth weight, IUGR) identified hypertension, active lupus nephritis, and thrombocytopenia as significant risk factors. Buyon et al. [17] recently demonstrated that lupus anticoagulant, antihypertensive medication use, thrombocytopenia, and high disease activity predict adverse outcomes. Moroni et al. [18] found that proteinuria and active lupus nephritis were associated with increased preterm delivery rates. Wagner et al. [19] reported higher rates of preterm delivery and fetal loss in pregnancies with active lupus nephritis compared with inactive disease, while no differences were observed between SLE patients without renal involvement and those with quiescent lupus nephritis. Our findings confirm that active lupus nephritis is an independent risk factor for adverse pregnancy outcomes, emphasizing the need for close monitoring of blood counts, blood pressure, and particularly urinalysis during pregnancy.

The risk of SLE flare increases two- to three-fold during pregnancy [20], with active disease elevating the risk of maternal complications [21-22]. In our cohort, approximately half (49%) of patients experienced disease activity during pregnancy. Reported hypertension rates in SLE pregnancies range from 15% to 23.6% [1,8,23]; our observed rate of 21.7% was consistent with this range, with significantly higher incidence in the moderate-severe activity group compared with the remission-mild activity group, suggesting that disease control may reduce hypertension risk. Preeclampsia/eclampsia represents another major maternal complication, with reported rates of 20%–28.4% in SLE pregnancies [23-25] associated with disease activity. Our study identified 7 cases (10.1%), lower than previous reports, with no significant difference between activity groups, possibly due to our limited sample size. One maternal death occurred at 16 weeks due to heart failure; this patient had multiple prior SLE flares, a history of adverse pregnancy outcomes, and had discontinued medications spontaneously, experiencing disease flare at 13 weeks. Clowse et al. [9] reported a maternal mortality rate of 0.32% in SLE pregnancies, 20 times higher than in the general population, highlighting the substantially increased mortality risk.

Few studies have characterized new-onset SLE during pregnancy. Limited data suggest that 63.1%–75% of patients with pregnancy-onset SLE develop disease in the first or second trimester, with 65.9%–68.8% developing lupus nephritis. These patients are more likely to experience renal and hematologic involvement, as well as interstitial pneumonia and thrombotic thrombocytopenic purpura [21,26-28]. In our study, all 15 cases of new-onset SLE occurred in the first or second trimester, with 9 (60%) developing lupus nephritis. Pregnancy outcomes

were poor, with fetal loss in 11 cases (73.3%), preterm delivery in 3 (20%), and full-term delivery in only 1 (6.7%). Management strategies for new-onset SLE during pregnancy remain poorly defined, warranting further investigation to improve outcomes in this high-risk subgroup.

This study has several limitations. Its retrospective design required exclusion of patients with incomplete data, resulting in a relatively small sample size that precluded stratified analysis. Additionally, we included only hospitalized SLE patients who delivered at our institution, likely representing a population with more severe disease that may not reflect the broader spectrum of SLE pregnancies. Future studies should consider incorporating outpatient data or multiple centers to enhance generalizability.

In summary, although most SLE patients can achieve successful delivery, the rates of maternal complications and adverse pregnancy outcomes remain concerning. We recommend that SLE patients conceive during periods of disease stability under multidisciplinary care, with regular monitoring, appropriate medication use, and optimal disease control to improve pregnancy outcomes and minimize maternal-fetal complications.

References

[1] Yan Yuen S, Krizova A, OuimetJM, et al. Pregnancy outcome in systemic lupus erythematosus (SLE) is improving: Results from a case control study and literature review [J]. Open Rheumatol J, 2008, 2(1): 89-98.

[2] Clark A, Spitzer A, Laskin A. Decrease in pregnancy loss rates in patients with systemic lupus erythematosus over a 40-year period [J]. J Rheumatol, 2005, 32(9): 1709-12.

[3] Wallenius M, Salvesen KA, DaltveitAK, et al. Secular trends of pregnancies in women with inflammatory connective tissue disease [J]. ActaObstetGynecolScand, 2015, 94(11): 1195-202.

[4] Cervera R, Font J, Carmona F, et al. Pregnancy outcome in systemic lupus erythematosus: good news for the new millennium [J]. Autoimmun Rev, 2002, 1(6): 354-9.

[5] Carvalheiras G, Vita P, Marta S, et al. Pregnancy and systemic lupus erythematosus: review of clinical features and outcome of 51 pregnancies at a single institution [J]. Clin Rev Allergy Immunol, 2010, 38(2/3): 302-6.

[6] Cortés-Hernández J, Ordi-Ros J, Paredes F, et al. Clinical predictors of fetal and maternal outcome in systemic lupus erythematosus: a prospective study of 103 pregnancies [J]. Rheumatology (Oxford), 2002, 41(6): 643-50.

[7] Moroni G, Doria A, Giglio E, et al. Maternal outcome in pregnant women with lupus nephritis. A prospective multicenter study [J]. J Autoimmun, 2016, 74(8): 194-200.

[8] Imbasciati E, Tincani A, Gregorini G, et al. Pregnancy in women with pre-existing lupus nephritis: predictors of fetal and maternal outcome [J]. Nephrol Dial Transplant, 2009, 24(2): 519-25.

[9] Clowse E, Jamison M, Myers E, et al. A National study of the complications of lupus in pregnancy [J]. Am J ObstetGynecol, 2008, 199(2): 127.e1-6.

[10] Molokhia M, Maconochie N, Patrick L, et al. Cross-sectional analysis of adverse outcomes in 1,029 pregnancies in Afro-Caribbean women in Trinidad with and without systemic lupus erythematosus [J]. Arthritis Res Ther, 2007, 9(6): R124.

[11] Bombardier C, Gladman DD, Urowitz MB, et al. Derivation of the SLEDAI. A disease activity index for lupus patients. The Committee on Prognosis Studies in SLE [J]. Arthritis Rheum, 1992, 35(6): 630-40.

[12] Madazli R, Yuksel A, Oncul M, et al. Obstetric outcomes and prognostic factors of lupus pregnancies [J]. Arch GynecolObstet, 2014, 289(1): 49-53.

[13] Clowse E, Magder S, Witter Frank, et al. The impact of increased lupus activity on obstetric outcomes [J]. Arthritis Rheum, 2005, 52 (2): 514-21.

[14] 高彦彦, 叶华, 郭衍秋, 等. 系统性红斑狼疮合并妊娠 49 例分析 [J]. 中华风湿病学杂志, 2012, 16(8): 553-6.

[15] 张红卫, 陈国强, 陈蔚瑜, 等. 系统性红斑狼疮对妊娠结局影响的病例对照研究 [J]. 中华风湿病学杂志, 2006, 10(5): 293-6.

[16] Chen Y, Chen H, Lin C, et al. Increased risk of adverse pregnancy outcomes for hospitalisation of women with lupus during pregnancy: a nationwide population-based study [J]. ClinExpRheumatol, 2010, 28(1): 49-55.

[17] Buyon JP, Kim M, Guerra MM, et al. Predictors of Pregnancy Outcomes in Patients With Lupus: A Cohort Study [J]. Ann Intern Med, 2015, 163(3): 153-163.

[18] Moroni G, Doria A, Giglio E, et al. Fetal outcome and recommendations of pregnancies in lupus nephritis in the 21st century. A prospective multicenter study [J]. J Autoimmun, 2016, 74(10): 6-12.

[19] Wagner SJ, Craici I, Reed D, et al. Maternal and foetal outcomes in pregnant patients with active lupus nephritis [J]. Lupus, 2009, 18(4): 342-7.

[20] Stojan G, Baer AN. Flares of systemic lupus erythematosus during pregnancy and puerperium: prevention, diagnosis and management [J]. Expert Rev ClinImmunol, 2012, 8(5): 439-53.

[21] Yang H, Liu H, Xu D, et al. Pregnancy-related systemic lupus erythematosus: clinical features, outcome and risk factors of disease flares–a case control study [J]. PLoS One, 2014, 9(8): e104375.

[22] Yang J, Chen Y, Chang H, et al. Pregnancy outcome of systemic lupus erythematosus in relation to lupus activity before and during pregnancy [J]. J

Chin Med Assoc, 2015, 78(4): 235-40.

[23] Kwok LW, Tam LS, Zhu T, et al. Predictors of maternal and fetal outcomes in pregnancies of patients with systemic lupus erythematosus [J]. Lupus, 2011, 20(8): 829-36.

[24] Liu J, Zhao Y, Song Y, et al. Pregnancy in women with systemic lupus erythematosus: a retrospective study of 111 pregnancies in Chinese women [J]. J Matern Fetal Neonatal Med, 2012, 25(3): 261-6.

[25] 宋亦军, 刘冬舟, 刘俊涛, 等. 妊娠合并系统性红斑狼疮 94 例临床分析 [J]. 中华内科杂志, 2008, 47(12): 1008-11.

[26] Zhao C, Zhao J, Huang Y, et al. New-onset systemic lupus erythematosus during pregnancy [J]. ClinRheumatol, 2013, 32(6): 815-22.

[27] Miyamoto T, Hoshino T, Hayashi N, et al. Preeclampsia as a manifestation of New-Onset systemic lupus erythematosus during pregnancy: a case-based literature review [J]. AJP Rep, 2016, 6(1): e62-7.

[28] Ku M, Guo S, Shang W, et al. Pregnancy outcomes in Chinese patients with systemic lupus erythematosus (SLE): A retrospective study of 109 pregnancies [J]. PLoS One, 2016, 11(7): e0159364.

Note: Figure translations are in progress. See original paper for figures.

Source: ChinaXiv —Machine translation. Verify with original.