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Original Article

Maternal and Fetal Outcomes in Patients with Systemic Lupus Erythematosus

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Abstract

Objectives: Lupus is associated with a considerable risk of fetal and maternal complications. The aim of this study was to assess the maternal and fetal outcomes in pregnant women with systemic lupus erythematosus (SLE) and likely predictors of adverse outcome in Benghazi, Libya. **Patients and Methods:** This was a retrospective review of the outcome of sixty pregnancies among 48 SLE patients attending the rheumatology clinics at Benghazi medical center, who were pregnant from January 2008 to December 2018. Each pregnancy was counted as a separate case. **Results:** The mean age to conceive was 30.6±6.1 years (19–42 years). Nineteen (31.7%) patients were primigravida, and the patients' age at SLE diagnosis was 25.2 ± 5.6 years. Forty-eight of the pregnancies (80%) were planned, ten patients have preexisting hypertension (HTN), most cases were in clinical remission before pregnancy (53 patients; 88%), only seven patients were identified as having active disease, four of them had lupus nephritis based on clinical features. Secondary antiphospholipid syndrome was diagnosed in four patients. Most pregnancies (50; 83%) resulted in live birth babies, 3 (5%) of them were preterm due to preeclampsia, six pregnancies (10%) ended in spontaneous abortion, and there were four intrauterine fetal deaths. More positive cases for aCl antibodies were affected than negative cases ($P = 0.005$). Five pregnancies complicated by preeclampsia, three of them have preexisting HTN, thirty patients (50%) underwent vaginal delivery, twenty patients (33%) underwent cesarean section due to different obstetric indications (previous cesareans and preeclampsia). Thirteen neonates (26%) were born with low birth weight, and two neonates (3%) required neonatal intensive care unit admission; no neonatal cases of lupus or congenital cardiac problems were reported. Postnatal SLE flare was reported among 16 patients (53%); preexisting HTN was strongly associated with preeclampsia, preterm labor, and postnatal SLE flares (*P*-values were 0.001, 0.003, and 0.004, respectively), whereas secondary Antiphospholipid antibody syndrome (APL) was associated with preeclampsia and abortion ($P = 0.005$ and 0.002). **Conclusion:** Preexisting HTN and secondary APL are associated with an increased risk of pregnancy complications. Characteristics and outcomes in our series are comparable to previously published international cohorts.

Keywords: Fetal outcomes, intrauterine fetal deaths, Libya, maternal, pregnancy, spontaneous abortion, systemic lupus erythematosus

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Introduction

Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disease that mainly affects women in the reproductive age group. SLE females have the same fertility rate as the age-matched population of healthy females.[1,2]

A better understanding of the pathogenesis of SLE and good use of immunosuppressive drugs allowed better control of the disease activity resulting in a remarkable improvement in the quality of life of these patients, including pregnancy outcomes.[3,4] Nevertheless, there is still a considerable risk of fetal and maternal complications.[5] Pregnancies for patients with SLE have a higher risk of fetal loss, intrauterine growth retardation (IUGR), prematurity, preeclampsia, higher mortality risk, and low birth weight (LBW) in addition to an increase in the disease activity itself.[6,7] Most of these complications are often difficult to distinguish from physiological changes or complications arising from pregnancy.[7]

There are limited data on SLE in pregnancy in our part of the world and the aim of this study was to assess adverse pregnancy outcomes and their likely predictors in women with SLE in Benghazi, Libya.

Patients and Methods

This was a retrospective cohort study of sixty pregnancies in 48 SLE female patients attending the rheumatology clinics at Benghazi Medical Center (Benghazi, Libya), whom conceived during the period of January 2008–December 2018. Each pregnancy was counted as a separate episode (case). All patients were >18 years' old and fulfilled at least 4 of the 11 criteria of the American College of Rheumatology.[8] Antiphospholipid syndrome (APS) was diagnosed according to the 2006 revised classification criteria.[9] Data collected included age, gravidity, parity, age at SLE diagnosis, duration of disease, pre- and postnatal SLE manifestations, current and past medications utilized, lupus activity before and after conception, and laboratory data. Investigations included antinuclear antibodies, anti-double-stranded DNA (dsDNA) antibodies, lupus anticoagulants, anticardiolipin antibodies via immunoglobulins G (aCL IgG) and M (aCL IgM). Anti-Ro/SSA and anti-La/SSB antibodies were also collected. Baseline routine laboratory tests (prenatal, natal, and postnatal) included complete blood picture, serum transaminases, alkaline phosphatase, serum albumin, creatinine, urine analysis, 24-h urine collection for total proteinuria, fasting and postprandial blood glucose, serum uric acid, and erythrocyte sedimentation rate were collected.

Pregnancy outcomes were assessed by the occurrence of obstetric complications including spontaneous abortion (a miscarriage in which the fetus is born before the 20th week of pregnancy), intrauterine fetal death (IUFD)(defined as fetal death at or after 20–28 weeks of pregnancy), IUGR (defined as fetal weight that is below the 10th percentile for gestational age as determined through an ultrasound), development of preeclampsia (defined as new-onset hypertension (HTN) and proteinuria after 20 weeks' gestation), preterm labor (before 37 weeks' gestation), and postnatal SLE flare. Neonatal outcome was assessed by live births (term and preterm), LBW (<2.5 kg at birth), neonatal deaths (within 28 days after delivery), neonatal lupus syndrome or congenital heart block, and admission to neonatal intensive care unit (NICU).

The disease activity of SLE was evaluated using the SLE disease activity index (SLEDAI). Active disease at conception was defined as the SLEDAI score + or > 2.[10] SLE flare was defined as worsening of disease during pregnancies or development of new manifestations. Fares included new or worsened cutaneous disease, arthritis, pleuritis, pericarditis, nephritis, hematological abnormalities as hemolytic anemia or platelet count below 60,000/lL, adding new drugs (hydroxychloroquine and/or azathioprine), hospitalization for SLE-related manifestations, and increased prednisone dose.

Descriptive statistics were used to summarize the data. Chi-square test was used to evaluate the impact of clinical and laboratory characteristics on maternal and fetal outcomes. Logistic analysis was used to study the predictors of adverse pregnancy outcome (defined as the occurrence of abortion, preeclampsia, prematurity, IUFD, or SLE flare).

Each pregnancy was considered as a separate observation. In all cases, $P < 0.05$ was considered to be statistically significant. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) 17.0 (SPSS; SPSS Inc., Chicago, IL, USA).

Results

We reviewed data of 78 cases; 18 were excluded from the study because of missing data about pregnancy, natal and postnatal clinical condition. The mean age of the patients at getting pregnant was 30.6 ± 6.1 years (19–42 years). Nineteen (31.7%) were primigravida, and 41 (68.3%) were multigravida. The duration of SLE before pregnancy was 8 ± 4.3 years (1.5–21 years). Patient's age at SLE diagnosis was 25.2 ± 5.6 years. Forty-eight pregnancies (80%) were planned, ten patients have preexisting HTN, most cases were in clinical remission before pregnancy as determined by SLEDAI index (53 patients; 88%), the other seven patients were labeled as active disease, and four of them have lupus nephritis. Secondary antiphospholipid syndrome was diagnosed in four patients. Forty patients were on oral prednisolone with dose less than 25 mg/day which was markedly reduced to <10 mg/day among 51 patients, most patients continue on fixed dose hydroxychloroquine 200 mg/day pre and postnatally, and there were 55 patients on azathioprine 100 mg/day that continued pre and postnatally on the same dose. Two patients were on intravenous pulse cyclophosphamide therapy 3 months before conception which was stopped during pregnancy, the number increased to seven patients postnatally; SLE clinical manifestations as well as medications pre and postnatal and autoantibodies profile are shown in Table 1.

Most pregnancies (50; 83%) resulted in live birth babies, three (5%) of them were preterm due to preeclampsia, six pregnancies (10%) ended by spontaneous abortion, and there were four IUFD, most of them were positive for aCl antibodies ($P = 0.003$ compared to patients with negative aCl antibodies).

Five pregnancies were complicated due to preeclampsia, in which three of them have preexisting HTN, 30 patients (50%) underwent vaginal delivery, and 20 patients (33%) underwent cesarean section due to different obstetric indications (previous cesareans, preeclampsia).

Table 1: Clinical characteristics of the study population

	Prenatal	Postnatal
Clinical manifestations (%)		
Articular	1 (1.6)	4 (6.6)
Nephritis	4 (6.6)	8 (13.3)
Serositis	0 (0)	1 (1.6)
Cutaneous	14 (23.3)	4 (6.6)
Hematological (anemia/thrombocytopenia)	9 (15)	10 (16.6)
Neurological	1 (1.6)	1 (1.6)
Medications (mean±SD)		
Prednisolone (mg/day)	25±5	7.5±5
Hydroxychloroquine (mg/day)	200	200
Intravenous cyclophosphamide, pulse therapy (patients)	2	7
Autoantibodies	**Mean(SD)**	
ANA (%)	49 (81.6)	
Anti-dsDNA (%)	46 (76.6)	
aCL-IgG (%)	32 (53.3)	
aCL-IgM (%)	28 (46.6)	
Anti-Ro (%)	1 (1.6)	
Anti-La (%)	0 (0)	

SD: Standard deviation, ANA: Antinuclear antibodies, dsDNA: Double stranded DNA, aCL-IgG: Anticardiolipin antibodies via immunoglobulins G, aCL-IgM: Anticardiolipin antibodies via immunoglobulins M

Thirteen neonates (26%) were born with LBW, and two neonates (3%) required NICU admission; there were no neonatal cases of lupus or congenital cardiac problems.

Postnatal SLE flare (occurs within three months after delivery) was reported among 16 patients, 8 of them developed nephritis based on clinical findings of hematuria, raised renal function test, and low complements level; renal biopsy was not done because it is not easily accessible in our country, except for one patient whom renal biopsy resulted in class III lupus nephritis; there was one patient developed severe serositis in the form of pericarditis and infective endocarditis confirmed by echocardiographic findings and cultures.

Preexisting HTN was strongly associated with preeclampsia, preterm labor, and postnatal SLE flares ($P = 0.001$, 0.003, and 0.004, respectively), whereas secondary APL was associated with preeclampsia and abortion ($P = 0.005$ and 0.002).

Discussion

We retrospectively reviewed sixty pregnancies, of which 47 pregnancies (78%) ended without major maternal or fetal complications. Our study showed that spontaneous abortion occurred in six pregnancies (10%). This is less than some other studies such as Eman *et al*.[11] in their review of 91 pregnancies in Egypt reported that spontaneous abortion was recorded in 15%; but slightly higher than another multicenter study conducted by Moroni *et al*.[12] which showed an incidence of 8.4%. Previously reported abortion incidence varied between 4% and 28%.[11-14]

In our study, the incidence of preterm labor was 5%, which is much low compared to that observed in a neighboring country reported by Eman *et al*.[11] in which incidence of priority was 13%. Other studies reported a wide range in priority incidence between 17% and 54%.[15,16]

Five pregnancies in the present study were complicated by preeclampsia, three of them have preexisting HTN (P = 0.001) and secondary APL (P = 0.005). Other retrospective studies reported a wide range of preeclampsia incidence 3%–26% in which HTN was demonstrated as a significant risk factor.[11,17]

There were no reported SLE flares during pregnancy in our cohort. However, SLE flare was reported among 16 cases (26.6%) within 3 months after delivery, 8 of them (10%) develop nephritis, and one patient developed severe serositis in the form of pericarditis and infective endocarditis.

Although there is still uncertainty about the exact effect of pregnancy on the course of SLE, several studies showed that pregnancy increaseds the incidence of SLE flares with rates up to 35%,[18,19] whereas others reported no difference.[20] A multicenter prospective trial assessing maternal outcomes of pregnant women with slightly active or inactive lupus nephritis before pregnancy reported that mild-to-moderate disease flares occurred in 18.3% and severe flares in 1.4% of pregnancies;[21] these findings were slightly higher than ours mentioned.

Adverse pregnancy outcomes were significantly associated with HTN and APL. In the present study, preexisting HTN was strongly associated with preeclampsia, preterm labor, and postnatal SLE flares (P = 0.001, 0.003, and 0.004, respectively), whereas secondary APL was associated with preeclampsia and abortion (P = 0.005 and 0.002). Older age at pregnancy and active disease before pregnancy were associated in our patients with increased risk of postnatal SLE flares (P = 0.004); some previous studies demonstrate that SLE patients with APS had almost two-fold increase in fetal loss when compared to SLE patients with negative APS,[22] although other studies correlated active lupus nephritis and younger maternal age to prematurity.[21]

Conclusion

Despite the improvements in pregnancy outcome of SLE pregnant patients, there is still adverse maternal and fetal outcomes. Preexisting HTN and secondary APL are associated with an increased risk of pregnancy complications. Our data are close to the generally reported in all the previous studies. There is an urgent need to further reduce the risk of lupus during pregnancy by implementing high-risk pregnancy clinics to ensure close monitoring and timely interventions.

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Authors' contribution

Equal contribution.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Compliance with ethical principles

The study was conducted according to the Declaration of Helsinki 1975. The study was approved by the scientific committee at Jamhorya hospital (475/2020 م ج ب). All the information was kept confidential, and no individual identifiers were collected.

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