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Original Research Article

Effect of systemic lupus erythematosus on pregnancy outcome: a study of 40 cases at a tertiary health care center

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ABSTRACT

Background: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease in which organs and cells undergo damage initially mediated by tissue-binding autoantibodies and immune complexes. SLE has an impact on various organ systems. Ninety percent of the patients are women of child-bearing age thus pregnancies and its outcomes are of particular importance among women with SLE. The current study aims to study the maternal and foetal outcomes in SLE patients and to identify the predictors of adverse maternal and foetal outcomes in pregnancy.
Methods: Data of 60 pregnancies of 40 female SLE patients from September 2019 to May 2021 in V. S. general hospital, Ahmedabad, were retrospectively reviewed. All the patients met the 2012 SLICC classification criteria for SLE. SLE disease activity in pre-pregnancy state and during pregnancy were retrospectively evaluated using SLE disease activity index-(SLEDAI), based on medical history, physical examination and immunological evaluation. SLE disease activity during the current non pregnant state was also calculated using SLEDAI.
Results: In our study carried out 3 years among 60 pregnancies, the disease flared up in 23 pregnancies (38.3%). Out of 60 pregnancies with SLE, there 17 (28.3%) unfavourable outcomes. Unfavourable outcomes were significantly higher in patients with SLE flare (14, 60.9%). Similarly, patients with lupus nephritis (8, 66.7%) had unfavourable outcome.
Conclusions: In spite of tertiary level care in the hospital, foetal loss is a significant risk in these patients, so proper periconceptional counselling should be done

Keywords: SLE, Maternal outcome, Fetal outcome, Pregnancy impact on SLE

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease in which cells and organs undergo damage by tissue-binding autoantibodies and immune complexes.[1] In majority of the patients, autoantibodies are present for a few years before the first clinical symptoms appears has an impact on various organ systems including musculoskeletal, cutaneous, renal, haematological, pulmonary, cardiac, gastrointestinal and ocular. Not all organ systems may be implicated simultaneously. Ninety percent of the patients are women of child-bearing age. As a consequence, pregnancies and its outcomes are of particular importance among women with SLE. Although advances in the treatment of SLE and obstetric complications for the past decades have allowed more women with SLE to achieve successful pregnancies, SLE still remains an important contributor to maternal and foetal morbidity and mortality. There are different factors predicting the adverse outcomes of pregnancy in patients with SLE including active disease activity at conception, lupus nephritis, presence of antiphospholipid antibodies (aPL Ab) and SLE flare in pregnancy. The current study aims to study the maternal and foetal outcomes in SLE patients

METHODS

Data of 60 pregnancies of 40 female SLE patients from September 2019 to May 2021 in V.S. General hospital, Ahmedabad, were retrospectively reviewed. All patients met the 2012 SLICC classification criteria for SLE. SLE disease activity in pre-pregnancy state and during pregnancy retrospectively evaluated using SLE-SLEDAI, based on medical history, PE and immunological evaluation. SLE disease activity during current non pregnant state was also calculated using SLEDAI.

Study period

The study was carried out for 18 months.

Table 1: SLICC criteria for classification of SLE 2.

Clinical manifestation	Immunological manifestation
Skin	
Acute, subacute cutaneous LE (photosensitive, malar, maculopapular, bullous)	ANA >reference negative value
Chronic cutaneous LE (discoid lupus, panniculitis, lichen planus-like, hypertrophic verrucous, chill blains)	
Oral or nasal ulcer	Anti-ds DNA >reference, if by ELISA 2x ref.
Non scarring alopecia	Anti-Sm
Synovitis involving ≥2 joints	Anti-phospholipid (any of lupus anti-coagulant, false positive RPR, anti-cardiolipin, anti-beta glycoprotein 1
Serositis (pleurisy, pericarditis)	Low serum complement (C3, C4 or CH50)
Renal	Positive direct coombs test in absence of hemolytic
Prot/Cr ≥0.5	Anemia
Rbc casts	
Biopsy	
Neurologic	
Seizures, psychosis, mononeuritis, myelitis, peripheral or cranial neuropathies, acute confusional state	-
Hemolytic anemia	
Leucopenia or	<4000/µl
Lymphopenia	<1000/µl
Thrombocytopenia	<1,00,000/µl

Site

The study was conducted at department of general medicine, V. S. general hospital and SVPIMSR, department of rheumatology, V. S. general hospital and SVPIMSR and department of obstetrics and gynaecology, V. S. general hospital and SVPIMSR

Inclusion criteria

Women diagnosed with SLE according to 2012 SLICC criteria for SLE. Women of reproductive age group (15-45 years).

Exclusion criteria

Women not diagnosed with SLE during the course of pregnancy. Women not giving consent for the study.

Renal biopsy read as systemic lupus qualifies for classification as SLE if any lupus autoantibodies are present, even if total criteria are fewer than 4.

RESULT

Majority of the pregnant SLE women were in the 26-to-30-year age group (19, 47.5%) followed by 19 to 25 years (12, 30.0%). Mean age of the patients was 27.9±5.06 years.

Table 2: Age wise distribution of patients.

Age group (year)	Frequency	Percentage (%)
19 to 25	12	30.0
26 to 30	19	47.5
31 to 35	4	10.0
36 to 40	5	12.5
Mean ± SD	27.9±5.06	

Table 3: Duration of disease.

Durations (Years)	Mean	SD
Duration of symptoms	4.0	2.09
Duration SLE diagnosed	3.1	1.83

Average duration of the symptoms of SLE in the patients was 4.0±2.09 years and the average duration of patients diagnosed with SLE was 3.1±1.83 years. It shows that patients consulted physician about 0.9 yrs after symptoms.

Table 4: SLE disease activity during pregnancy.

Variables	SLE disease activity, n (%)		Total	P value
	Inactive	Active		
Pre pregnancy	44 (73.3)	16 (26.7)	60 (100)	0.17
Pregnancy	36 (60)	24 (40)	60 (100)	

In the pre pregnant state, only 16 (26.7%) women had active SLE. During pregnancy, the proportion of active SLE increased up to 40% but it was not statistically significant (p=0.17).

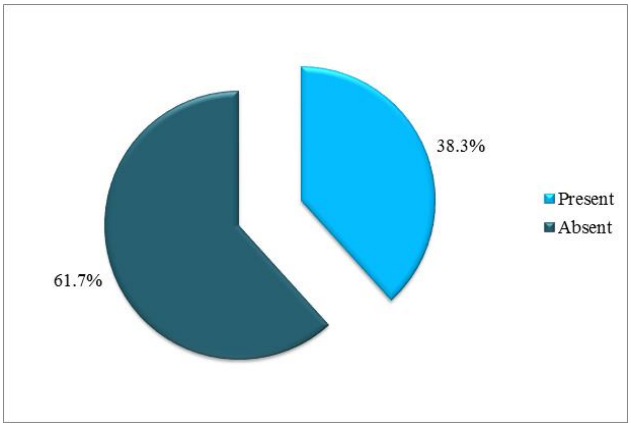

Figure 1: Occurrence of SLE flare in pregnancy.

SLE flare is referred to disease activity changing from inactive to active, or becoming more severe, requiring changes in therapy. Out of 60 pregnancies, flare was observed in 23 patients (38.3%).

Table 5: Factors associated with SLE flare in pregnancy.

Factors	SLE flare, (n=23) (%)	No SLE flare, (n=37) (%)	P value
Lupus nephritis in pregnancy			
Present (n=12)	11 (91.7)	1 (8.3)	<0.001
Absent (n=48)	12 (25)	36 (75)	
SLE disease activity in pregnancy			
Active (n=24)	23 (95.8)	1 (4.2)	<0.001
Inactive (n=36)	0 (0)	36 (100)	

Among 60 pregnancies, the disease flared up in 23 pregnancies (38.3%). Out of 12 pregnancies with lupus nephritis, 11 flared up (91.7%) which was higher in comparison with pregnancies without lupus nephritis (12/38, 25.0%, p<0.001). SLE disease flare was observed in the 95.8% of pregnancies with active SLE disease activity, whereas there was no flare observed in pregnancies with inactive SLE disease activity.

Table 6: Incidence of fetal outcome.

Pregnancy outcome		Total, (n=60) (%)
Live birth (48, 79.0%)	Healthy	43 (71.7)
	Preterm delivery	4 (6.7)
	Neonatal death	1 (1.6)
Fetal loss (12, 20.0%)	Abortion	9 (15)
	Still birth	3 (5)

Out of a total of 60 pregnancies, 48 (79.0%) were live births. Of them, 43 (71.7%) were healthy, 4 (6.7%) pre term births and 1 (1.6%) death occurred during the neonatal period (neonatal death). There 9 abortions (15.0%) and three (5.0%) were still birth.

Table 7: Factors associated with unfavourable outcome of pregnancy.

Variables	Favourable outcomes, (n=43) (%)	Unfavourable outcomes, (n=17) (%)	P value
SLE flare in pregnancy			
Present (n=23)	9 (39.1)	14 (60.9)	P<0001, RR=0.42 (0.25 to 0.71)
Absent (n=37)	34 (91.9)	3 (8.1)	
Lupus nephritis in pregnancy			
Positive (n=12)	4 (33.35)	8 (66.7)	P=0.002, RR=0.41 (0.18 to 0.92)
Negative (n=48)	39 (81.3)	9 (18.8)	
SLE disease activity in pregnancy			
Active (>4) (n=24)	10 (41.7)	14 (58.3)	P<0001, RR=0.45 (0.28 to 0.73)
Inactive (≤4) (n=36)	33 (89.2)	3 (10.8)	
Secondary APLA			
Present (n=4)	1 (25)	3 (75)	P=0.03, RR=0.33 (0.06 to 1.83)
Absent (n=56)	42 (75)	14 (25)	

Unfavourable outcomes were significantly higher in patients with SLE flare (14, 60.9%) as compared to patients without SLE (3, 8.1%). Similarly, patients with lupus nephritis (8, 66.7%) had unfavourable outcomes as compared to patients without lupus nephritis (9, 18.8%). Active SLE had significant negative impact on pregnancy outcome. [Unfavourable outcome in active SLE v/s inactive SLE: 58.3% v/s 10.8%, p<0.001].

Table 8: Association between unfavourable outcome and SLE flare.

Outcomes	SLE flare pregnant female, n (%)	Non flare pregnant female, n (%)	RR and p value
Un-favourable	14 (49.9)	3 (7.9)	RR=0.32 (95% CI=0.20 to 0.55), p=0.001
Abortion	(25.9)	(5.3)	
Still birth	3 (11.1)	(0.0)	
Neonatal death	1 (3.7)	(0.0)	
Preterm birth	3 (11.1)	1 (2.6)	
Live births	13 (48.1)	35 (92.1)	

Unfavourable outcomes were significantly higher in pregnant women with SLE flare (14, 49.9%) as compared to women without SLE flare (7.9%). Relative risk was 0.32 (95% CI=0.20 to 0.55).

DISCUSSION

In the present study, nearly half of the patients were in the 26-to-30-year age group with mean age of the patients was 27.9±5.06 years. Average duration of SLE was 4.0±2.09 years and average duration of patients diagnosed with SLE was 3.1±1.83 years. It was thus deduced that patients consulted physicians about 0.9 years after symptoms.

Eman et al studied pregnancy outcome of 91 pregnancies in 84 pregnant SLE patients at Cairo university, Egypt from October 2010 to January 2015.[1] Age of patients was similar to the present study, being 28.6±4.4 years however; duration of SLE disease was higher than the present study (7.6±5.1 years). Liu et al conducted a retrospective study among 111 pregnancies of 105 SLE patients in Peking union medical college China.[3] The mean age at pregnancy in their study was 29.2±4.2 years and the mean interval between diagnosis of SLE and pregnancy 4.9±4.2 years.

In the present study, the incidence of active disease in the pre-pregnant state was 26.7%, which increased to 40% during pregnancy. It implies that SLE disease activity in the present study increased during pregnancy from 26.7% to 40.0% but was not statistically significant (p=0.17). There are conflicting results of the impact of pregnancy on SLE activity, with some studies reporting no increased risk of SLE flares during pregnancy compared with controls while others found pregnancy to be associated with increased SLE flare rate compared with control.[7-11] Aly et al reported SLE flare up in 44.0% pregnancy. An independent review by Liu et al reported that SLE activity increased from 16.2% during conception to 36.3% during pregnancy.[1,3] Some researchers reported increased SLE activity during pregnancy.[10-11] However, others showed decreased or stable activity.

In the present study, pregnancy was successful in 48 women with SLE (79.0%). Of them, 71.7% were healthy, 6.7% were pre term births and 1.6% death occurred during the neonatal period. Rate of fetal loss including neonatal death was 21.6%. [Abortion 15.0%, still birth 5.0% and 1.6%]. We did not observe any IUGR in our study.

Variable results have been reported on fetal loss of 8-43% in retrospective series and 11-28% in prospective studies.[13,15-23,27] Incidence of abortion in SLE pregnancies was reported between 11% and 24%.[24] Prematurity rate in SLE pregnancies ranges between 17% and 54%.[28] Studies reported an incidence of live births in SLE pregnancies of 72-89%.[25] While other studies reported a much lower incidence between 45% and 50%.[29]

Liu et al reported that there were 25 abortions, and 5 stillbirths, with 81 pregnancies resulting in live births including two multiple gestations.[3] Three neonatal deaths were reported. Fetal loss rate including neonatal death was 11.1%. More than 3/4th live birth was observed in the Eman et al study.[1] There were 15% abortion, 32% IUGR, 13% preeclampsia, 8% IUFD, and 13% preterm birth, 3.0% neonatal death in the Eman et al study.[1]

In the present study, proportion of adverse pregnancy outcome was more in pregnancy with SLE flare (43.4%) than pregnancy without SLE flare (2, 5.4%, p=0.006). Active SLE, lupus nephritis and secondary APLA also had an adverse effect on fetal outcome. [Lupus nephritis v/without lupus nephritis: 66.6% v/s 8.3%, p<0.001; active SLE v/s Inactive SLE: 41.7% v/s 5.5%, p=0.009; positive for secondary APLA v/s negative for secondary APLA: 75.0% v/s 16.1%, p=0.002].

Liu et al reported their results which were comparable with our study.[3] [Active SLE v/s Inactive SLE: 17.0% v/s 2.9%, 0.04]. Preterm birth was also higher in active SLE group (53.2%) as compared to inactive SLE group (8.8%, p<0.001) in their study. Small for gestational age was also more frequent in active SLE group (40.0%) compared to the inactive group (5.6%, p<0.001).

Various studies reported a higher incidence of premature births in lupus pregnancy varying from 17% to 49%.[18-21] Our study failed to demonstrate such relationship. Incidence of preterm birth was 6.7%. Risk of preterm birth was not associated with SLE flare, lupus nephritis and active stage of SLE in our study. [Preterm birth, SLE flare v/s no flare: 13.1% v/s 2.70%, p=0.14; preterm birth in lupus nephritis v/s without lupus nephritis: 0.0% v/s 8.3% p=0.40; Preterm birth in active SLE v/s inactive SLE: 12.5% v/s 2.7%, p=0.29]. Liu et al demonstrated a higher incidence of preterm birth (34.6%).[3]

CONCLUSION

On the basis of the present study, we conclude that; pregnancies can be successful in most women with SLE. However, SLE activity can be significantly increased in a significant number of patients, even though well controlled. Adverse pregnancy outcome (including abortion, still birth, preterm birth, and neonatal death) increases significantly with SLE flares during pregnancy, active disease activity in pregnancy, lupus nephritis. Lupus nephritis, SLEDAI score (for SLE disease activity and flare) should be closely monitored during pregnancy. In spite of tertiary level care in the hospital, foetal loss is a significant risk in these patients, even if SLE is not clinically active at the time of conception. This information should be included in preconception counselling to guide women and their physicians in decision making related to future pregnancies.

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