Pregnancy outcome in systemic lupus erythematosus patients: A case series

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ABSTRACT

Systemic lupus erythematosus (SLE) is an autoimmune disorder that mainly affects reproductive age group women. Pregnancy may worsen SLE; especially, is associated with nephritis and SLE may lead to various pregnancy complications. Here, we present a series of eight known cases of pregnant women with SLE nephritis; of which 6 were booked and 2 cases were unbooked. Histological grading of renal involvement of the patients was done according to the World Health Organization classification/2004 classification of International Society of Nephrology/Renal Pathology Society. SLE activity in each patient was assessed using SLE disease activity index-2K. All cases were followed up to delivery and 12 months thereafter. It was found that the booked cases who conceived during disease remission had favorable outcomes, whereas, the unbooked cases had a disease flare during pregnancy leading to poor outcomes. Pregnancy should only be attempted after proper planning and disease remission in patients with SLE.

Key words: *Disease activity, Pregnancy, Systemic lupus erythematosus*

Systemic lupus erythematosus (SLE) is a chronic, multisystem autoimmune disease that occurs predominantly in women of reproductive age [1]. Pregnancy induces dramatic immune and neuroendocrine changes in the maternal body to protect the fetus from immunologic attack and these modifications can be affected by SLE. Previous studies have shown that an association of SLE and pregnancy, mainly with active disease and especially with nephritis, has poorer pregnancy outcomes. There are increased chances of preeclampsia, fetal loss, prematurity, fetal growth restriction, small for gestational age babies, and neonatal lupus.

Pregnancy, on the other hand, may increase disease activity and results in lupus flare or active nephritis, which has the potential for accelerated end-stage renal disease. Therefore, SLE during pregnancy is considered a high-risk condition from both maternal and fetal aspect [2,3]. For a favorable pregnancy outcome, prenatal care of pregnant patients with SLE requires close collaboration between rheumatologist, obstetrician, pediatrician, sonologist, and biochemist in a tertiary care centre [4-6]. This case series aims to document the maternal and fetal outcomes in pregnant women with SLE.

CASE REPORT

All known cases of SLE, attending the antenatal clinic or admitted to the antenatal ward over a period of 1 year from 2012 to 2013 in the Department of Obstetrics and Gynecology in a Medical College, Kolkata, were studied. All the cases were followed up for maternal and fetal outcomes. There were eight patients, six were booked (cases 1-6) and had a planned pregnancy, i.e. conceived after disease remission. Two cases were unbooked (cases 7 and 8) and had an unplanned pregnancy, conceived during active disease. All 8 patients had lupus nephritis (LN), diagnosed using American College of Rheumatology criteria (1997 Update of the 1982 American College of Rheumatology Revised Criteria) for classification of SLE.

Histological grading of renal involvement of the patients was done according to the World Health Organization classification [7]/2004 classification of International Society of Nephrology/Renal Pathology Society as follows: Class I - minimal mesangial LN; Class II - mesangial proliferative LN; Class III - focal LN; Class IV - diffuse LN; Class V - membranous LN; and Class VI - advanced sclerosing LN.

At the first visit, the previous medical, obstetric, and treatment history were recorded and clinical examination and necessary serological evaluations (namely antinuclear antibody [ANA], anti-ds DNA antibodies [IgM and IgG], anti-cardiolipin antibodies [IgM and IgG], anti-β2 glycoprotein-I [IgM and IgG], anti-SSA Ab, anti-SSB Ab, and C3 and C4) were carried out. SLE activity in each patient was assessed using SLE disease activity index-2K before pregnancy/at first visit and at the end of each trimester to monitor the SLE activity.

Active nephritis was considered if the patients had any one of the following at admission: >0.5 g proteinuria in a 24-h urine sample or red blood cell casts in urine. Cases 1-6 were followed up regularly in the gynecology and obstetrics OPD and the medicine OPD during the antenatal period and admitted at 32 weeks of conception for safe confinement. Cases 7 and 8 were

admitted through the emergency. After admission, all 8 patients were followed closely till delivery and post-delivery disease monitoring was continued up to 12 months. As this was a case series and no intervention was done, ethical committee clearance and patient consent were not needed.

The baseline features and clinical characteristics of all patients are summarized in Table 1. Cases 2, 3, 5, and 6 were primigravida while cases 1 and 4 had previous three and four spontaneous abortions, respectively, before being diagnosed with SLE. Case 6 had a history of myocarditis and neuropsychiatric manifestations leading to her diagnosis of SLE but showed no such symptoms after conception. Cases 1–6 did not show any sign of disease activity after conception as evident from negative test results (anti-ds DNA, anti-Ro/La, ANA, serum urea, and serum creatinine). Preeclampsia developed only in case 4. In other cases, the blood pressure was normal throughout pregnancy as shown in Table 2.

The pregnancy outcomes have been tabulated in Table 3. All 6 patients delivered live-born babies by lower segment cesarean section (LSCS), two of them being low birth weight due to preterm prelabor rupture of membranes, necessitating emergency LSCS. No sign of neonatal lupus in the form of cutaneous manifestations or congenital heart block was seen in any of the babies at birth and also at 6 weeks follow-up.

Cases 7 and 8 were unbooked cases and were admitted through emergency at 34 and 28 weeks of gestation, respectively. The patients had signs of active SLE such as a malar rash (Fig. 1), oral ulcers, proteinuria and microscopic hematuria and raised serum urea, and creatinine levels at presentation. Case 7 presented with less fetal movement, no signs of pregnancy-induced hypertension (PIH) was seen. Ultrasonography for fetal viability showed intrauterine fetal death. Case 8 developed PIH along with SLE flare at 36 weeks requiring an emergency cesarean section. There was no evidence of deep vein thrombosis in any of the cases. The microscopic image of glomerulonephritis and skin changes is shown in Figs. 2 and 3.

DISCUSSION

In this case series, we found that pregnancy outcome was the best when patients conceived during remission phase and had proper antenatal care. Fertility rates are normal in women with

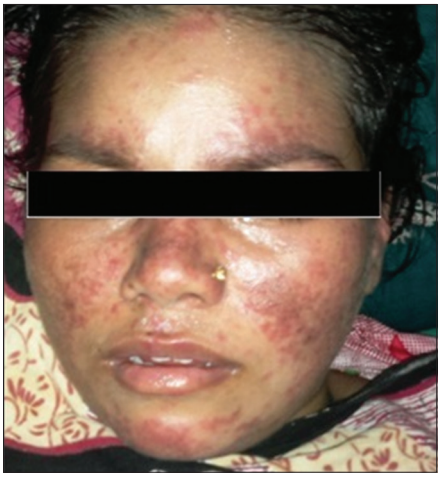

Figure 1: Butterfly rashes seen in the face of the patient with systemic lupus erythematosus

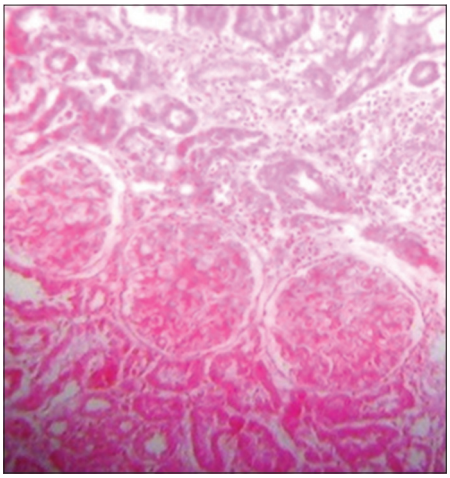

Figure 2: Microscopic image of glomerulonephritis

Table 1: Demography of the patients (*n*=8)

Case	Age (years)	Married for (in years)	Gravida and parity	Lab data pre-conception	WHO class of SLE nephritis	Duration since diagnosis (years)	T/t (pre-conception)
1 (B)*	19	2	$G_1 P_{0+3}$		II (MPGN)	2	Steroid(↑dose) +ACE-I
2 (B)	21	2	$G_1 P_{0+0}$		II (MPGN)	2	-do-
3 (B)	22	2	$G_1 P_{0+0}$	ANA+	IV (DPGN)	5	-do-+Azathioprine
4 (B)	31	8	$G_5 P_{0+4}$	APLA+ANA+	V (MGN)	3	Steroid(↑dose)+ACE-I
5 (B)	24	3	$G_1 P_{0+0}$		II (MPGN)	2	-do-
6 (B)	26	6	$G_1 P_{0+0}$		III (focal GN)	5	Steroid (↑dose)+Cyclophosphamide
7 (UB)#	27	9	$G_7 P_{1+5}$ (LI-nil)		Kidney biopsy not available	1	Steroid (↑dose)+HCQS (discontinued)
8 (UB)	23	8	$G_3 P_{1+1}$ (LI-1)		Kidney biopsy not available	2	Steroid (↑dose)+HCQS

***B: Booked, #UB: Unbooked, MPGN: Membranoproliferative glomerulonephritis, DPGN: Diffuse proliferative glomerulonephritis, MGN: membranous glomerulonephritis, ANA: Antinuclear antibody, SLE: Systemic lupus erythematosus, WHO: World Health Organization**

Table 2: Treatment received

Case	Admission		BP	s/s	Urine RE/ME		Lab data (on admission)	T/t (post-conception)
	Via	POG (week)			Proteinuria	RBC/Casts		
1 (B)	OPD	32	N		Trace	Nil	WNL	Steroid (↓dose), Aspirin (↓dose)
2 (B)	OPD	32	N		Trace	Nil	WNL	-do-
3 (B)	OPD	32	N		Trace	Nil	WNL	-do- + Azathioprine
4 (B)	OPD	32	N initially↑after 36w	H/O DVT	1+	Nil	↑ESR APLA-positive	Steroid (↓dose), Aspirin (↓dose), LMWH
5 (B)	OPD	35	N		1+	Nil	WNL	Steroid (↓dose), Aspirin (↓dose)
6 (B)	OPD	32	N		Trace	Nil	WNL	Steroid (↓dose), Aspirin (↓dose)
7 (UB)	ER	34	N	Malar rash, Oral ulcer, less fetal movement	1+	RBC+>5/hpf	↑anti-dsDNA↑anti-Ro/ La antibody C3-WNL APLA-negative↑Se urea, Creatinine	-do-
8 (UB)	ER	28	N initially; ↑after 34 week	Malar rash, oral ulcer, psychosis	1+	RBC+>5/hpf	↑dsDNA, ↑ESR CRP, C3-WNL↑Se urea, creatinine	-do-

B: Booked, UB: Unbooked, RBC: Red blood cell, ESR: Erythrocyte sedimentation rate, CPR: C-reactive protein

Table 3: Outcome of treatment

Case	Pregnancy complications	POG at delivery (weeks)	Mode of delivery	Live/still born	Birth weight (kg)	Apgar score (1 min)	Neonatal complication
1 (B)	None (H/O- BOH)	38	LSCS'	Live	2.9	9	None
2 (B)	None	38	LSCS	Live	2.6	9	None
3 (B)	PPROM	35	LSCS	Live	2.2	6	RDS
4 (B)	PET, PPROM	36	LSCS	Live	2.25	6	RDS
5 (B)	None	37	LSCS	Live	2.4	9	None
6 (B)	None	38	LSCS	Live	2.7	9	None
7 (UB)	IUFD	34	VD	Stillborn (macerated)	1.25	_	_
8 (UB)	Preecalmpsia	37	LSCS	Live	2.0	5	RDS, Sepsis

B: Booked, UB: Unbooked, LSCS: Lower segment cesarean section, IUFD: Intrauterine fetal death, RDS: Respiratory distress syndrome, PPROM: Premature rupture of membranes

SLE. However, pregnancy in the background of SLE is prone to complications and hence, must be considered at high risk [8]. Prognosis for both mother and child is best when SLE is quiescent for at least 6 months before the pregnancy [9,10], and the mother's renal function is stable. LN can get worse during pregnancy. In a previous case series of 86 cases, the maternal outcome is worst in active nephritis [11]. Pregnancy loss is more likely if SLE is diagnosed during the index pregnancy or if patient conceives before the disease is in remission.

In our study, 6/8 of the cases were planned pregnancies conceived after at least 6 months of disease quiescence. They had good maternal and fetal outcome with proper medication and careful monitoring. No evidence of SLE flare or any other maternal complications were seen, except for the development of preeclampsia in one patient. Following delivery, treatment was continued as per pre-pregnancy schedule. Patients were followed up after 6 weeks and at 3 monthly intervals for a year thereafter. No evidence of neonatal lupus or maternal disease flare was seen in any of the cases.

Case 7 was an unplanned pregnancy with poor patient compliance resulting in flare-up of SLE and pregnancy loss. Following delivery, treatment was continued as per pre-pregnancy schedule and patient was advised not to conceive until after 6 months of disease remission. Case 8 was also an unplanned pregnancy, conceived during active disease. But compliance to medications and vigilant maternal and fetal monitoring led to early diagnosis and management of complications (like PIH) and a successful pregnancy outcome. Following delivery, treatment was continued as per pre-pregnancy schedule. She was discharged after control of disease flare and followed up for a year. The postpartum period was uneventful.

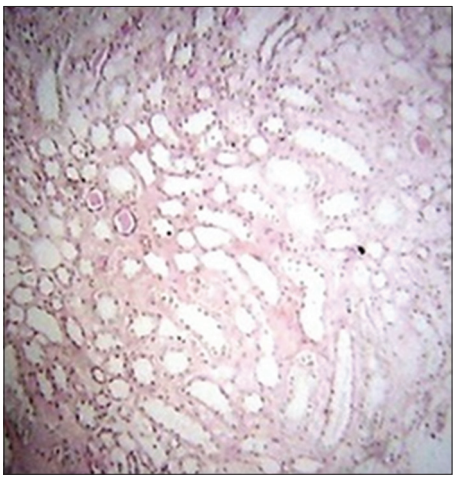

Figure 3: Microscopic picture of skin changes

In our study, the use of azathioprine (as seen being used in case 3) was not associated with teratogenicity in a patient with SLE in pregnancy. Some studies have suggested that exposure to azathioprine during pregnancy is not associated with poor fetal outcome [10-12]. The main limitation of this study is that the number of cases is very small. We are presently continuing the study and hope to come up with more number of cases in the future.

CONCLUSION

A planned pregnancy after disease remission is an essential pre-requisite for successful pregnancy outcome in SLE patients. Regular antenatal care and fetal monitoring are essential, especially in anti-Ro, anti-La positive patients. Early diagnosis of complications and their prompt management and optimal timing of delivery are essential for good maternal and fetal outcome.

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