ARP Rheumatology 2025;4:66-68
https://doi.org/10.63032/RMXO6650

LETTERS TO THE EDITOR

Pregnancy outcomes in systemic sclerosis: experience of a rheumatology-obstetric multidisciplinary clinic

Chícharo AT[1,2,3], Lopes AR[1,2], Barreira S[1,2], Martins P[1,2], Cruz-Machado AR[1,2], Pinto L[4,5], Capela S[1,2]

Dear editor,

Systemic sclerosis (SSc) is a rare multisystemic connective tissue disease (CTD). It is mainly characterized by progressive fibrosis and non-inflammatory vasculopathy. Women diagnosed with SSc seem to be at increased risk of developing adverse pregnancy outcomes (APO), but maternal and perinatal outcomes remain poorly understood in these patients, with no data yet available from Portuguese centers[1,2].

With this work, we aim to describe maternal and perinatal outcomes in women with SSc. APO were defined as the presence of (1) miscarriage if pregnancy loss < 10 weeks of gestation; (2) fetal death if > 10 weeks of gestation; (3) neonatal death if within the first 28 days of life; (4) congenital abnormalities; (5) preeclampsia or eclampsia; (5) preterm birth; (6) fetal growth restriction or (7) small for gestational age and (8) neonatal infections if within the first 28 days of life.

A monocentric retrospective observational study was performed, including pregnant women with SSc followed at a rheumatology-obstetric multidisciplinary clinic from 01/2009 to 03/2023.

Overall, a total of 12 pregnancies in 9 patients with SSc were identified. Disease phenotypes included: 1 diffuse cutaneous SSc (dcSSc), 3 limited cutaneous SSc (lcSSc), 2 very early diagnosis of systemic sclerosis (VEDOSS), 2 SSc sine scleroderma (ssSSc) and 1 overlap syndrome of SSc and dermatomyositis with predominance of SSc manifestations. Six women were positive for anti-centromere antibodies, while three others exhibited anti-Scl-70. Two women had positive anti-SSA/SSB antibodies; all had negative antiphospholipid antibodies. Only one patient had major organ involvement – a case of usual interstitial pneumonia (UIP) in a woman with ssSSc. Table I summarizes maternal clinical data and pregnancy outcomes. The mean age at conception was 35.9 ± 4.9 years with a median disease duration of 19 (IQR 8.5) years. All women followed in our unit had their disease stable at the time of conception under no teratogenic drugs. Additionally, all performed echocardiogram and pulmonary function tests (PFT) during preconception period and/or during pregnancy: none had high probability of pulmonary hypertension according to estimated systolic pulmonary arterial pressure; and only the patient with UIP had an isolated reduction on DLCO on PFT. Out of the 12 pregnancies, there were 10 live births and 2 miscarriages [at 4 and 6 weeks of gestation (WG)]. The mean gestational age at delivery was 38.2 ± 1.8 WG. There was one preterm birth at 35 WG in the woman with ssSSc with UIP after spontaneous preterm premature rupture of membranes (PPROM). Fetal growth restriction was diagnosed at 35 WG in a woman with lcSSc, and three other babies were born small for gestational age (SGA), from mothers with VEDOSS, lcSSc and ssSSc. There were no cases of gestational hypertension or pre-eclampsia. Two patients underwent scheduled cesarean sections for reasons not related to their CTD. No congenital abnormalities, neonatal infections or neonatal lupus cases were recorded. All women decided to breastfeed. During gestation, all women experienced improvement in their Raynaud phenomenon (RP), except for a patient with lcSSc who developed digital ulcers that improved with nifedipine 30mg/day, and calcinosis in elbows and fingers that persisted in the postpartum period. There were also frequent complaints of gastroesophageal reflux in 3 (33%) patients who had preexisting gastroesophageal symptoms. The patient with ssSSc with UIP reported a dry cough at 27th WG. After exclusion of respiratory tract infection, she was diagnosed with alveolitis related to her underlying lung disease. Prednisolone was increased up to 10mg/day and her symptoms improved. It was then gradually tapered to 5mg before delivery at 35 WG due to PPROM. A postpartum relapse occurred in one patient with dcSSc, marked by worsening RP, inflammatory arthralgia, and aggravated skin thickening of the hands and feet. Regarding immunomodulatory treatment, 4 patients (44%) were under conventional DMARDs (azathioprine and hydroxychloroquine) and 3 (33%) women received prednisolone (Table I). No associations were found between disease phenotype,

[1] Rheumatology and Metabolic Bone Diseases Department, Hospital de Santa Maria, Unidade Local de Saúde de Santa Maria, Lisbon, Portugal
[2] Instituto Gulbenkian de Medicina Molecular João Lobo Antunes, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal
[3] Rheumatology Department, Unidade Local de Saúde do Algarve, Hospital de Faro, Portugal
[4] Department of Obstetrics, Gynecology and Reproductive Medicine, Hospital de Santa Maria, Unidade Local de Saúde de Santa Maria
[5] Faculty of Medicine of University of Lisbon, Lisbon, Portugal

Submitted: 07/01/2025
Accepted: 20/02/2025

Correspondence to: Ana Teodósio Chícharo
E-mail: anatzchicharo@gmail.com

TABLE I. Maternal rheumatic disease characteristics and pregnancy outcomes in women with systemic sclerosis followed at a rheumatology-obstetric clinic.

Patient	Pregnancy	Disease phenotype	Clinical manifestations	Major organ involvement	Antibodies profile	Disease duration at conception (in years)	Obstetric history	csDMARD at conception	csDMARD during pregnancy	Other drugs during pregnancy	Gestation age at delivery (in WG)	Birth weight (grams)	Adverse pregnancy outcomes	Disease flares during pregnancy	Disease flares during post -partum
A	1	Diffuse cutaneous SSc	RP, puffy fingers, digital ulcers, arthritis	No	Anti-Scl 70	9	G2P1A0	0	0	Nifedipine 20mg daily	-	-	Miscarriage at 4th WG	-	-
	2					10	G3P1A1	0	Hydroxyclo-roquine 400mg daily	Nifedipine 20mg daily, AAS 150mg daily	40	3320	0	0	Yes (worsening of RP, inflammatory arthralgia and aggravated skin thickening)
B	3	Limited cutaneous SSc	RP, puffy fingers, inflammatory arthralgia, GER	No	Anti-centromere, Anti-SSA/SSB	7	G1	Hydroxyclo-roquine 400mg daily	Hydroxyclo-roquine 400mg daily	AAS 150mg daily, PDN 2.5mg daily	37	2720	0	0	0
C	4	Limited cutaneous SSc	RP, sclerodactyly, telangiectasia	No	Anti-centromere	3	G2A0P1	0	0	0	37	2355	Fetal growth restriction	0	0
D	5	Limited cutaneous SSc	RP, digital ulcers, calcinosis cutis, telangiectasia	No	Anti-centromere	18	G1	0	0	0	39	3300	0	0	0
	6					25	G2P1A0	0	0	Nifedipine 20mg daily	41	3300	0	Yes (worsening of RP, digital ulcers and calcinosis)	
E	7	VEDOSS	RP, puffy fingers, arthritis	No	Anti-centromere	4	G1	Hydroxyclo-roquine 400mg daily	Hydroxyclo-roquine 400mg daily	AAS 150mg daily	39	2920	SGA	0	0
F	8	VEDOSS	RP, puffy fingers, calcinosis cutis	No	Anti-centromere	8	G2P1A0	0	0	AAS 150mg daily	-	-	Miscarriage at 6th WG	-	-
	9					10	G3P1A1	0	0	AAS 150mg daily	39	3980	0	0	0
G	10	Sine scleroderma SSc	RP, puffy fingers, GER, dysphagia	No	Anti-centromere	14	G2P1A0	0	0	AAS 150mg daily	37	2330	SGA	0	0
H	11	Sine scleroderma SSc	RP, puffy fingers, GER, interstitial lung disease	Yes - UIP	Anti-Scl 70	6	G2P1A0	Azathioprine 125mg daily	Azathioprine 125mg daily	PDN 5-10mg daily	35	2820	Preterm delivery with PPROM	Yes (alveolitis)	0
I	12	Overlap of SSc and DM	RP, digital ulcers, sclerodactyly, calcinosis, gottron papules, heliotrope rash, polymyositis	No	Anti-Scl 70, Anti-SSA/SSB	10	G2P1A0	Hydroxyclo-roquine 400mg daily	Hydroxyclo-roquine 400mg daily	AAS 150mg daily, PDN 2.5 mg daily	38	2635	SGA	0	0

AAS - acetylsalicylic acid, GER - gastroesophageal reflux; PDN - prednisolone; PPROM - preterm premature rupture of membranes; SSC – systemic sclerosis; SGA - small for gestational age; UIP – usual interstitial pneumonia; VEDOSS – Very early diagnosis of systemic sclerosis; WG - weeks of gestation

auto-antibodies profile or disease flares and the risk of APO. However, the small sample size limits the ability to draw robust conclusions.

To the best of our knowledge, this is the first study to describe pregnancy outcomes in women with SSc followed in a Portuguese center. Documenting these results is crucial for enhancing care planning for women with SSc. While the majority of women with SSc managed at our clinic experienced successful gestations, the risk of APO and disease flares underscores the need for a close follow-up. Our findings align with existing literature, which reports an increased rate of APO in these patients, (although the risk of miscarriages is still controversial) and a stable disease throughout pregnancy in most cases. This work highlights the importance of a multidisciplinary approach to empower and support women with rare CTD throughout their reproductive journey.

REFERENCES

1. Blagojevic J, AlOdhaibi KA, Aly AM, Bellando-Randone S, Lepri G, Bruni C, Moggi-Pignone A, Guiducci S, Mecacci F, Matucci-Cerinic M, Furst DE. Pregnancy in Systemic Sclerosis: Results of a Systematic Review and Metaanalysis. J Rheumatol. 2020 Jun 1;47(6):881-887. https://doi.org/10.3899/jrheum.181460
2. Lazzaroni MG, Crisafulli F, Moschetti L, et al. Reproductive Issues and Pregnancy Implications in Systemic Sclerosis. Clinical Reviews in Allergy & Immunology. 2023 Jun;64(3):321-342. https://doi.org/10.1007/s12016-021-08910-0