



# Pre pregnancy counselling in lupus- Rheumatologist perspective

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# Overview

- Introduction-Pre pregnancy counselling
- Impact of lupus on pregnancy
- Impact of pregnancy on lupus
- Fetal complications
- Special situations- LN,APS,RO positive mothers in lupus
- Medication use in pregnancy
- Recommendations

# Introduction

- Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disease predominantly affecting women, particularly those of childbearing age.
- Pre-pregnancy counselling is the pivotal first step in the management of SLE patients with a wish to become pregnant.
- Pre pregnancy counseling is to prepare patients desiring children for adequate monitoring and management during pregnancy.

# Introduction

- Planning a pregnancy means finding the right time and right conditions with low disease activity and therapy adjusted to pregnancy-compatible drugs.
- Multidisciplinary approach to pre-pregnancy counselling in SLE patients is mandatory.
- Maternal and fetal risks in SLE pregnancy can be anticipated with an integral, patient-tailored (pre-)pregnancy treatment plan.

# Pre pregnancy counselling in lupus



# Introduction

- Prenatal counseling requires risk assessment regarding
  - ❑ Maternal or fetal risks,
  - ❑ Screening for biomarkers with predictive value for adverse pregnancy outcomes,
  - ❑ Therapy adjustment
  - ❑ Schedule for monitoring and follow-up during pregnancy.
  
- Counseling on birth control is necessary to avoid unplanned pregnancies, which carry high maternal and fetal risks.

# Risk factors to consider in women with SLE during pre pregnancy counselling

SLE-related risk factors	General risk factors
✓ Active SLE in the previous 6–12 months or at conception	✓ Maternal age
✓ Active/history of Lupus Nephritis	✓ Arterial hypertension
✓ End-stage organ damage	✓ Diabetes mellitus
✓ Vascular thrombosis	✓ Overweight or obesity
✓ Previous adverse pregnancy outcome	✓ Thyroid disease
✓ Serological activity (C3, C4 levels, and antidsDNA titre)	✓ Smoke and alcohol use
✓ aPL profile (LA, aCL IgG/IgM, a $\beta$ 2GPI IgG/IgM)	✓ Immunization status (eg, rubella)
✓ Anti-Ro/SSA, anti-La/SSB antibodies	

## Systemic lupus erythematosus pregnancy evaluation and monitoring

Pre-pregnancy	Every 6–8 weeks <sup>a</sup>
Complete blood count with platelets	Complete blood count with platelets
Comprehensive metabolic panel	Comprehensive metabolic panel
Prothrombin time/partial thromboplastin time	Urinalysis with microscopy
Urinalysis with microscopy	Spot protein/creatinine ratio
24-h urine protein and creatinine clearance <sup>b</sup>	Anti-ds DNA
Spot protein/creatinine ratio	Complement levels (C3, C4)
Anti-ds DNA	Uric acid
Anti-Ro/SS-A and La/SS-B antibodies	
Lupus anticoagulant <sup>c</sup>	
Anticardiolipin IgG, IgM, IgA <sup>c</sup>	
Anti- $\beta$ 2 glycoprotein I IgG, IgM, IgA <sup>c</sup>	
Complement levels (C3, C4)	
Uric acid	

# Pre pregnancy consultation

- A clinical work-up and laboratory tests will show the presence of risk factors for a future pregnancy, and will allow a stratification into a high-, moderate- or low-risk profile.



1 <sup>st</sup> group	2 <sup>nd</sup> group	3 <sup>rd</sup> group
1 <sup>st</sup> group	2 <sup>nd</sup> group	3 <sup>rd</sup> group
Advised to go for pregnancy	Advised to postpone till remission	Maternal/fetal risks explained, in certain situations avoid pregnancy

## High maternal risk situations for pregnancy in systemic lupus erythematosus

Avoid pregnancy if:

Severe pulmonary hypertension (systolic pulmonary artery pressure >50 mm Hg)

Severe restrictive lung disease (forced vital capacity <1 L)

Advanced renal insufficiency (creatinine level >2.8 mg/dL)

Advanced heart failure

Previous severe preeclampsia or HELLP (hemolysis, elevated liver enzyme levels, low platelet count) despite therapy

Stroke within the previous 6 months

Severe disease flare within last 6 months

# Impact of lupus on mother and fetus

- Maternal /fetal risks during pregnancy can be
  - ❑ Maternal (lupus flares, worsening renal impairment, onset of or worsening hypertension, preeclampsia, or venous thromboembolism [VTE])
  - ❑ Fetal–neonatal risks (miscarriage, intrauterine growth restriction [IUGR], preterm delivery, neonatal lupus syndrome)
- The principal predictors of adverse pregnancy outcomes include active SLE, LN, hypertension, proteinuria, thrombocytopenia, and the presence of aPL.
- Many of the reported pregnancy outcomes are derived from SLE patients that had quiescent disease for at least 6 months, recommended by international recommendations.

Bertsias G, Ioannidis JP, Boletis J et al. EULAR recommendations for the management of systemic lupus erythematosus. Report of a task force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics. *Ann Rheum Dis* 2008;67:195-205.

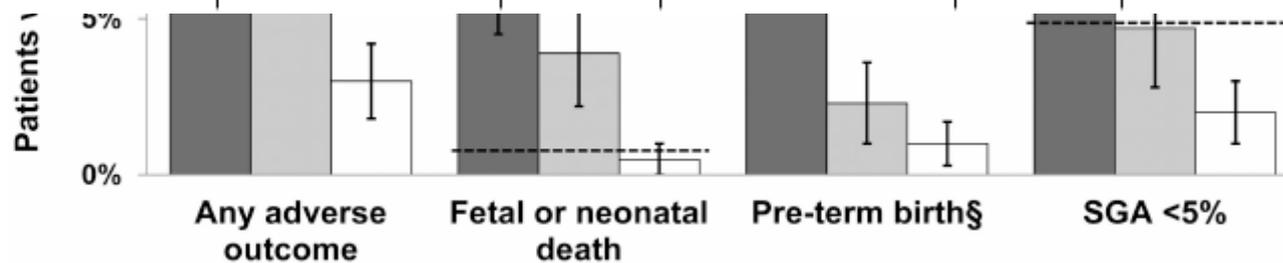
# Evidence-pre pregnancy counselling

- **First prospective inception cohort** by Buyon et al. reported on the outcome of **385 SLE pregnancies** from the Predictors of pRegnancy Outcome: bioMarkers In antiphospholipid antibody Syndrome and Systemic lupus Erythematosus (**PROMISSE**) study.
- **PROMISSE cohort encompassed pre-pregnancy counselling.**
- SLE patients with confirmed low or no disease activity -81% of patients conceived without an adverse pregnancy outcome.

Buyon JP, Kim MY, Guerra MM et al. Predictors of pregnancy outcomes in patients with lupus: a cohort study. Ann Intern Med 2015;163:15363.

	Model 1: APO at any time during pregnancy (N=385, Events = 73)	Model 2: APO after 23 weeks (N=370, Events = 62)	Model 3: APO after 35 weeks (N = 318, Events = 30)
20-23 weeks			
Flare:			
Mild/Moderate vs None		3.14 (1.25-7.90)	0.0150
Severe vs None		5.87 (1.15-29.96)	.033
Change in C3 from baseline (per 0.10 g/L decrease)		1.24 (1.03-1.50)	0.025
SLEPDAI (per 2 point increase)		1.43 (1.06-1.94)	0.020

32-35 weeks				
Flare:				
Mild/Moderate vs None			1.95 (0.55-7.00)	0.30
Severe vs None			9.60 (1.95-47.35)	0.006



Buyon JP, Kim MY, Guerra MM et al. Predictors of pregnancy outcomes in patients with lupus: a cohort study. *Ann Intern Med* 2015;163:15363.

# Overview of reported pregnancy outcomes in the investigating SLE patients

	Meta-analysis		Case-control study				Case-control study				Prospective cohort study			
	<i>Smyth et al. CJASN 2010 [11]</i>		<i>Clowse et al. AJOG 2008 [4]</i>				<i>Arkema et al. A&amp;R 2016 [9]</i>				<i>Buyon et al. AIM 2015 [10]</i>			
	37 1842 2751	Studies Patients Pregnancies	Cases: 13,555 SLE pregnancies	Controls: 16.7 mln non-SLE pregnancies			Cases: 551 SLE pregnancies	Controls: 12,847 non-SLE pregnancies			385 SLE patients			
Influence of pregnancy on SLE disease	SLE flares	26%	NR <sup>a</sup>				NR <sup>a</sup>				SLE flares	24%		
	Hypertension	16%									Mild	20%		
	Nephritis	16%									Severe <sup>b</sup>	4%		
	ESRD	0%												
Influence of SLE on pregnancy	Induced abortion	6%		(%)	(%)	OR		(%)	(%)	OR				
	Preeclampsia	8%	Preeclampsia	23	vs	8	3.0	Preeclampsia	16	vs	4.7	NR	Preeclampsia	16%
	Pregnancy fail <sup>c</sup>	23%	Eclampsia	0.5	vs	0.1	4.4							
	Miscarriage	16%	Preterm labor	21	vs	8	2.4	Preterm labor	23	vs	6.5	NR	Preterm labor	8%
	Foetal/neonatal death	7%	C-section	37	vs	25	1.7	C-section	35	vs	16	NR		
	IUGR	13%	IUGR	23	vs	8	3.0	IUGR	15	vs	3.7	NR	IUGR	9%
			Maternal- Death	0.3	vs	0.01	18.0							
			Thrombosis	1.7	vs	0.08	10.0							
		Infection	2.2	vs	0.3	3.9								
Influence of SLE on neonate/foetus	Foetal death	4%	Foetal death	NR							Foetal death	5%		
	Neonatal death	3%	Neonatal death	NR							Neonatal death	1%		
	IUGR	13%	IUGR	23	vs	8%	3.0	IUGR	15	vs	3.7	NR	IUGR	9%

# Overview of pregnancy outcome in retrospective, single-centre or referral cohort studies, depicted are absolute numbers (%)

Publication	No. of pregnancies	Influence of pregnancy on SLE disease	Influer	Influence of SLE on neonate/foetus		
		SLE flare	Miscarriages/ abortion	Foetal/neonatal death	Prematurity	IUGR or SC
LUMINA	102	NR	41 (40)	5 (4.9)	19 (19)	NR
Nili <i>et al.</i> [82]	97	NR	NR	1 (1.0)	NR	17 (18)
Cavallasca <i>et al.</i> [83]	72	17 (24)	5 (6.9)	3 (4.2)	33 (46)	24 (39)
Carvalheiras <i>et al.</i> [84]	51	16 (31)	3 (5.9)	2 (3.9)	8 (16)	NR
Jakobsen <i>et al.</i> [85]	84	39 (46)	21 (26)	1 (1.2)	38 (45)	10 (12)
Sun Ko <i>et al.</i> [15]	183	92 (51)	17 (9.3)	12 (6.6)	48 (26)	24 (13)
Park <i>et al.</i> [86]	62	13 (33)	9 (15)	2 (3.2)	13 (21)	9 (15)
Koh <i>et al.</i> [87]	183	81 (44)	12 (6.6)	4 (2.2)	61 (33)	48 (26)
Chen <i>et al.</i> [88]	1010	NR	NR	NR	145 (14)	288 (29)
Ku <i>et al.</i> [89]	109	NR	NR	42 (39)	NR	47 (43)
Yang <i>et al.</i> [90]	155	41 (26)	30 (19)	7 (4.5)	36 (23)	NR
Jiaxuan <i>et al.</i> [91]	52	26 (50)	NR	NR	NR	NR
Liu <i>et al.</i> [92]	111	26 (23)	25 (23)	18 (16)	28 (25)	24 (22)
Chen <i>et al.</i> [93]	83	27 (33)	20 (24)	5 (6.0)	11 (13)	7 (8.4)
Teh <i>et al.</i> [94]	115	30 (26)	28 (24)	11 (9.6)	23 (20)	16 (17)
Teh <i>et al.</i> [95]	48	17 (35)	10 (21)	3 (6.3)	8 (17)	11 (23)
Ideguchi <i>et al.</i> [96]	55	38 (69)	11 (20)	2 (3.6)	13 (24)	22 (52)
Madazli <i>et al.</i> [97]	65	5 (7.7)	NR	3 (4.6)	7 (11)	12 (19)
Al Arfaj <i>et al.</i> [98]	383	118 (31)	94 (25)	20 (5.2)	64 (17)	60 (16)
<b>Overall</b>	<b>3020</b>	<b>586/1702 (34)</b>	<b>326/1687 (19)</b>	<b>141/1958 (7.2)</b>	<b>555/2814 (20)</b>	<b>619/2660 (23)</b>

# Disease activity –Flares in pregnancy

Disease status	Flare risk
Active disease within 6 months prior to pregnancy	58%
>6 months quiescent disease prior to pregnancy	8%

**A SLEDAI of 4 in the 6 months preceding conception was identified as a threshold above which the flare rate increased during pregnancy.**

M. E. B. Clowse, L. S. Magder, F. Witter, and M. Petri, "The impact of increased lupus activity on obstetric outcomes," *Arthritis and Rheumatism*, vol. 52, no. 2, pp. 514–521, 2005.

Gladman DD, Tandon A, Ibanez D, Urowitz MB. The effect of lupus nephritis on pregnancy outcome and fetal and maternal complications. *J Rheumatol* 2010;37:7548.

# Fetal complications

- It is well known that SLE can have a negative impact on fetal pregnancy outcome.
- Placental dysfunction due to shallow invasion of the syncytiotrophoblast originates very early in pregnancy, in the first trimester.
- SLE patients are at increased risk for fetal intrauterine death, mainly before fetal viability (<24weeks of gestation) is achieved.
- IUGR complicates up to one in four SLE pregnancies.

# SLE-Preterm birth

## Systemic lupus erythematosus and risk of preterm birth: a systematic review and meta-analysis of observational studies

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We performed a meta-analysis to identify the association between systemic lupus erythematosus (SLE) and preterm birth. In this study, we studied the effects of SLE, SLE disease activity, a history of nephritis and active nephritis on preterm birth. Searches were conducted before 20 May 2016 of PubMed, Embase, Medline and Cochrane Library of literature and article reference lists. Eleven observational case-control studies and thirteen cohort studies met the inclusion criteria. The pooled relative risk (RR) for the risk of preterm birth in SLE patients versus controls was 2.05 (95% confidence interval (CI): 1.72–3.32); for active SLE patients versus inactive was 2.98 (95% CI: 2.32–3.83); for SLE patients with a history of lupus nephritis versus those without nephritis it was 1.62 (95% CI: 1.35–1.95); and for SLE patients with active nephritis versus those with quiescent nephritis it was 1.78 (95% CI: 1.17–2.70). In summary, this study identified a significant association in the above results. This association was more significant in active SLE patients versus inactive. With respect to SLE itself, active inflammation (such as disease activity) may be more hazardous for the management of the pregnancy. This suggests that it is essential to control disease activity in order to achieve a better outcome of SLE pregnancy. *Lupus* (2017) 0, 1–9.

# Lupus nephritis and pregnancy

- The principal considerations for pregnant women with lupus nephritis are:
  - 1) Effect of the pregnancy on disease status, both during the pregnancy and on long-term renal function
  - 2) Effect of lupus nephritis on pregnancy outcome.
- Adverse obstetric outcomes need to be quantified for the woman. (PIH, lupus flare)
- Meta-analysis of 37 studies with 1,842 patients showed that prior nephritis was associated with higher rates of preeclampsia
- Fetal loss along with risks of preterm delivery /IUGR should be discussed.

# Lupus nephritis and pregnancy

- History of LN increased the risk of an SLE flare during pregnancy by 3-fold.
- Women with quiescent disease (proteinuria <500mg/day and inactive urinary sediment) and unaffected renal function are at reasonably low risk during pregnancy but should be closely monitored.
- Establishing baseline blood tests pre-pregnancy or in early pregnancy will aid in identification of a flare or developing pre-eclampsia.
- Tandon A, Ibanez D, Gladman DD, Urowitz MB. **The effect of pregnancy on lupus nephritis.** *Arthritis Rheum.* 2004;**50**:3941-3946

# Lupus nephritis and pregnancy

- All pregnancies in women with lupus nephritis should be planned, preferably after more than six months of quiescent disease.
- Predictors of poor obstetric outcome include active disease pre-pregnancy or early pregnancy; baseline poor renal function with Cr >100 mmol/L; proteinuria >0.5 g/24 hours; presence of concurrent APS; or hypertension.
- Patients with CKD and an estimated GFR of 545 ml/min should be reassured that the risk for ESRD is probably not increased and is comparable to that of healthy

K Bramham, MC Soh and C Nelson-Piercy **Pregnancy and renal outcomes in lupus nephritis: an update and guide to management** *Lupus* 2012 21: 1271

Zhang JJ, Ma XX, Hao L et al. **A systematic review and meta-analysis of outcomes of pregnancy in CKD and CKD outcomes in pregnancy.** *Clin J Am Soc Nephrol* 2015;10:196478.

# SLE with APS

- 30–50% of SLE patients have aPL, but only one-third show the clinical picture of the APS with obstetric or thrombotic events
- Women with aPL are in general at a higher risk for hypertension, pre-eclampsia, fetal death, placental insufficiency with growth restriction and prematurity.
- Women with consistent moderate-to high levels of aPL or APS must be informed about the risk of thrombosis, pregnancy loss and pre-eclampsia, as well as the necessity of anticoagulation during pregnancy and postpartum.

# SLE with APS

- The PROMISSE study observed a 3-fold increase in adverse pregnancy outcomes in SLE patients with secondary APS (44%) compared with SLE patients without secondary APS (15%).
- In women with definite obstetric APS, combination treatment with LDA and heparin is recommended to decrease the risk of adverse pregnancy outcomes.
- SLE patients with aPLs without established APS have no indication for anticoagulant treatment during pregnancy.

Mak A, Cheung MW, Cheak AA, *et al.* Combination of heparin and aspirin is superior to aspirin alone in enhancing live births in patients with recurrent pregnancy loss and positive anti-phospholipid antibodies: a meta-analysis of randomized controlled trials and meta-regression. *Rheumatology (Oxford)* 2010;49:281–8.

Cohen D, Berger SP, Steup-Beekman GM, Bloemenkamp KW, Bajema IM. Diagnosis and management of the antiphospholipid syndrome. *BMJ* 2010;340:c2541.

# SLE Mothers with anti RO positivity

- SLE-related autoantibodies (anti-SSa/SSb autoantibodies) can cross the placenta and induce NLE in the fetus.
- Most severe manifestation is congenital heart block
- Congenital heart block is characterized by fetal bradycardia and an atrioventricular block that develops during weeks 18-24 of pregnancy, coinciding with the time that immunoglobulins can cross the placenta.
- Detection of an early conduction defect such as a prolonged PR interval should be considered a danger signal.

# Neonatal lupus-CHB

- Low risk (0.7–2%) for CHB in women with no previous CHB
- It is unclear whether intensive monitoring (weekly/biweekly between 16 and 26 weeks of gestation and less frequently afterwards) is cost-effective.
- CHB associated with anti-Ro/SSA and/or anti-La/SSB has 16% recurrence rate in women with a previously affected child; therefore, it is recommended to perform serial fetal echocardiograms weekly from 16 weeks of gestation onwards.
- There is no proven efficacy of protocols for the prevention or treatment of complete CHB.

Brito-Zerón P, Izmirly PM, Ramos-Casals M, *et al* The clinical spectrum of autoimmune congenital heart block. *Nat Rev Rheumatol* 2015;**11**:301–12.

Saxena A, Izmirly PM, Mendez B, *et al* Prevention and treatment in utero of autoimmune-associated congenital heart block. *Cardiol Rev* 2014;**22**:263–7.

# Lupus Inheritance

- Common question from SLE patients is whether the disease is inherited by future children?
- Genome-wide association studies have identified 30 genes accounting for 10% of the heritability of SLE.
- The rates of concordance are 24-56% in monozygotic twins and 14% in dizygotic twins, with an heritability index estimated at 66%.
- A Danish population study showed a 6% incidence of SLE in offspring from parents with SLE.

Incidence of SLE in the general population is very low, the absolute risk for an SLE patient to conceive a child with SLE is negligible and patients can therefore be reassured

# Contraception

- Counseling on birth control is the only way to prevent unplanned and ill-timed pregnancy.

Method of birth control	Safety–failure rate at perfect/typical use (%)	Recommended for patients with characteristics
<b><i>Combined hormonal contraception containing estrogen plus progestin (for patients with mild/moderate and stable disease activity, no aPL, no APS)</i></b>		
Combined oral contraceptives containing 15–35 µg estrogen	0.3–8.0	All ages of premenopausal SLE patients
Hormonal patch	0.3–8.0	Patients who do not want another pill
Vaginal ring	0.3–8.0	Patients who do not want another pill
<b><i>Progestin only (for patients positive for aPL or with APS; patients with very active and severe SLE)</i></b>		
Progestin-only pills	0.5–8.0	Patients who have good compliance
Implant	0.1	Patients who do not want another pill or with poor compliance
Injection of medroxyprogesterone	0.3	Patients with poor compliance Be aware of amenorrhea and osteoporosis
<b><i>IUD (possible for all patients including those positive for aPL or with APS, or with active and severe SLE)</i></b>		
Copper IUD	0.1–0.8	Patients who do not want another pill or with poor compliance Patients dependent on low cost of birth control
Levonorgestrel IUD	0.1–0.8	All patients, particularly suited for patients on anticoagulation
<b><i>Sterilization</i></b>		
Female sterilization	0.1	Reserve for women who have completed their families

# Medications

Commonly used therapies in SLE are analgesics, immunosuppressive medication, antihypertensives and anticoagulation medication.

Many of these compounds are not compatible with pregnancy because of the associated risk of embryopathies, miscarriage or negative impact on second and third trimester development.

Discontinue before conception	Continue during pregnancy when indicated	Start with
Methotrexate	Antimalarials	Folic acid
Cyclophosphamide	Prednisone	Vitamin D plus calcium
Rituximab	Azathioprine	Aspirin for prevention of pre-eclampsia
Belimumab	Cyclosporine	
Tocilizumab	Tacrolimus	
Mycophenolate mofetil		
Angiotensin-converting enzyme inhibitors		
Bisphosphonates		
Coumarin derivatives	Low-molecular weight heparin	Switch from coumarin derivatives to low-molecular weight heparin

Pregnant women with SLE at risk of PE, in particular those with LN and aPL positivity or APS, should start LDA preconceptionally or no later than 16 week of pregnancy

Studies of pregnant SLE patients have shown that the risk of a flare during pregnancy is reduced in women continuing with AM throughout pregnancy

Reduce frequency of CHB in Anti Ro positive lupus mothers

Cortes-Hernandez J, Ordi-Ros J, Paredes F, Casellas M, Castillo F, Vilardell-Tarres M. Clinical predictors of fetal and maternal outcome in systemic lupus erythematosus: a prospective study of 103 pregnancies. *Rheumatology (Oxford)* 41, 643–650 (2002)

# EULAR Recommendation -2017

**Table 1** Recommendations for women's health and the management of family planning, assisted reproduction, pregnancy and menopause in patients with systemic lupus erythematosus (SLE) and/or antiphospholipid syndrome (APS)

Statement/recommendation	LoA	
	Mean (SD)	Median (IQR)
1. Preconception counselling and risk stratification	10 (0.2)	10 (0)
1.1 In women with SLE, major risk factors for adverse maternal and fetal outcomes include active/flare SLE (1/A), especially active nephritis (1/A), history of lupus nephritis (2/B) and presence of aPL/APS* (1/A).		
1.1.1 Blood pressure monitoring (2/B), use of safe medications to control disease activity (emphasis on HCQ (2/B)) and limiting glucocorticoids exposure (2/B) are essential measures.		
1.2 In women with APS (primary or SLE-APS), risk factors include high-risk aPL profile (lupus anticoagulant, multiple aPL, moderate to high titre aPL) (1/A), coexisting SLE (2/B), history of vascular/thrombotic APS (2/B) and of previous adverse pregnancy complications (2/B).		
1.2.1 Blood pressure monitoring (3/C) and use of antiplatelet and/or anticoagulant therapy ( <i>rated at statement 9</i> ) are of fundamental importance.		

## Checklist of parameters to be considered for preconception counselling and risk stratification in women with systemic lupus

<i>Disease-related risk factors</i>	<i>Prognostic implications</i>
SLE activity/flares* (in the last 6–12 months or at conception)	Increased risk for (i) maternal disease activity (RR 2.1 for subsequent flare during pregnancy and puerperium); <sup>14</sup> (ii) hypertensive complications (OR 1.8 for PE); <sup>15</sup> (iii) fetal morbidity and mortality (OR 5.7 for pregnancy loss, <sup>16</sup> 3.5 for IUGR <sup>17</sup> 6.5 for preterm delivery) <sup>14 15 17–22</sup>
Lupus nephritis (history or active at conception)	Strong predictor of poor maternal (RR 9.0 for renal flare during/after pregnancy) <sup>23</sup> and fetal outcome(s) (OR 7.3 for fetal loss and 18.9 for preterm delivery) <sup>24 25</sup>
Serological (serum C3/C4, anti-dsDNA titres) activity	Increased risk for maternal SLE flares during pregnancy (OR 5.3) <sup>14</sup> and pregnancy loss <sup>23 26 27</sup>
Previous adverse pregnancy outcome(s)	APS: increased risk for pregnancy complications <sup>28–30</sup>
History of vascular thrombosis	APS: increased risk (ORs ranging 3.6–12.7) for pregnancy morbidity <sup>31</sup>
SLE diagnosis	APS: increased risk (OR 6.9) for pregnancy morbidity <sup>31 32</sup>
aPL profile‡	SLE: strong predictor of adverse maternal and fetal outcomes, <sup>19 25 27 33 34</sup> especially for patients with persistent moderate-to-high aPL titres, LA and multiple aPL positivity (high-risk aPL profile) APS: high-risk aPL profile correlates with increased risk of maternal vascular thrombotic events during pregnancy (OR 12.1), <sup>35</sup> (pre-)eclampsia (OR 2.3), <sup>36 37</sup> APS-related pregnancy morbidity (OR 9.2), <sup>31</sup> IUGR (OR 4.7), <sup>36</sup> preterm birth <sup>38 39</sup>
Anti-Ro/SSA, anti-La/SSB antibodies	Linked to development of neonatal lupus, including a low risk (0.7–2%) for CHB (especially if moderate-to-high anti-Ro titres); <sup>40–43</sup> weak association with other pregnancy complications <sup>44</sup>

# EULAR Recommendation -2017

2. Contraceptive measures 9.9 (0.4)
- 2.1 Women with SLE should be counselled about the use of effective contraceptive measures (oral contraceptives, subcutaneous implants, IUD), based on their disease activity and thrombotic risk (particularly aPL status). IUD can be offered to all the patients with SLE and/or APS free of any gynaecological contraindication (1/A).
- 2.2 In patients with stable/inactive SLE and negative aPL, combined hormonal contraceptives can be considered (1/A). In women with positive aPL with or without definite APS, hormonal contraception (with progesterone only) must be carefully weighed against the risk of thrombosis (2/B).
3. Risk factors for reduced fertility 9.8 (0.4)
- Women with SLE who wish to plan a pregnancy should be counselled about fertility issues, especially the adverse outcomes associated with increasing age and the use of alkylating agents (1/A). Treatment with alkylating agents should be balanced against the risk of ovarian dysfunction.
4. Preservation of fertility 9.5 (0.7)
- Fertility preservation methods, especially GnRH analogues, should be considered for all menstruating women with SLE who are going to receive alkylating agents (2/B).

# Prepregnancy evaluation for patients with SLE.

## Evaluate for high-risk situations (Box 1)

- Advise against pregnancy if present

## Evaluate disease activity

- Discuss contraception if active disease and defer pregnancy
- Proceed with pregnancy planning if stable for at least 6 months

## Risk stratify based on disease activity and autoantibody profile (aPL and anti-Ro/La antibodies)

## Individualized multidisciplinary plan for management based on risk profile

## Optimize medications and counsel patient on the need to continue safe medicines

# Conclusions

- Preconception counselling is crucial in women with SLE.
- Preconception counselling and risk stratification (based on disease activity and serological profile) are key points for having successful pregnancies.
- Disease activity at conception and in prior 6 months is a predictor of adverse pregnancy outcomes.
- Conception should be advised at a stage of remission or minimal disease activity and on stable medications.
- Maternal and fetal outcomes with active vs inactive disease at conception should be discussed.

# Conclusions

- Contraceptive methods should be discussed at times of active disease to prevent unplanned pregnancies.
- Although 60% of pregnancies will have normal pregnancy outcome, one of five patients will have PE and preterm birth in 20-30%.
- To establish appropriate medication use .
- If Immunosuppressive regimen is changed it is recommended to evaluate its efficacy for 4-6 months to ascertain stable disease control before conception.

# Conclusions

- Multidisciplinary pre-pregnancy counselling will result in an integral, patient-tailored treatment plan for the pre-conception, pregnancy, delivery and postpartum periods.

# References

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- Vagelli R, Tani C, Mosca M Pregnancy and menopause in patients with systemic lupus erythematosus and/or antiphospholipid syndrome. Practical messages from the EULAR guidelines. Pol Arch Intern Med.2017 Jan 25;127(2):115-121.
- Andreoli L, Bertias GK, Agmon-Levin N et al EULAR recommendations for women's health and the management of family planning, assisted reproduction, pregnancy and menopause in patients with systemic lupus erythematosus and/or antiphospholipid syndrome. Ann Rheum Dis. 2017 Mar;76(3):476-485.

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Thank  
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