



# **Time to Pregnancy in Women with SLE**

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# Disclosures

- **None**

# Background

- **There is a general notion that patients with SLE have a fertility rate comparable to that of the general population**
- **This viewpoint might be challenged for several reasons:**
  - **Of the 9% infertile women worldwide, SLE contributes to ~1% , which is more than would be expected for a disease affecting ~0.05% of women**

# Background

- **Vinet et al., *Ann Rheum Dis*, 2012:**
  - **Large population-based study in Quebec**
  - **Compared with the general population, live births were substantially lower after SLE diagnosis (SIR 0.62; 95% CI 0.55 to 0.70) than before diagnosis (SIR 1.01; 95% CI 0.90 to 1.13)**

# Background

- **Many factors can impair fertility rates in SLE women:**

cause	General consequences	Effects on reproductive function
Age	Pregnancy reported after Flare Free, Reduced number of follicles, low ovarian reserves	Anovulatory Cycles
High disease activity	pain, stiffness, Fatigue	Reduced libido and Frequency of intercourse
Disease-Related	Autoimmunity causes POF, Infection: STI - CMV, menstrual disturbance, APS, CRF	hypothalamic–pituitary dysfunction , low fertilization, impaired implantation
Treatment	NSAID :Luteinized unruptured follicle syndrome, Cyclophosphamide gonadotoxic, Glucocorticoids: Cushing's syndrome	Anovulatory Cycles
Psychosocial	Anxiety to change therapy and fear of a disease flare during pregnancy, perceived difficulties with child caring, couple dysfunction	Choice to limit family size

# Background

- **Time to pregnancy (TTP):**
  - **Measures the time (in months) required to conceive in subjects actively trying**
  - **Consistently shown to be a sensitive measure of fertility**
  - **Can be assessed either retrospectively or prospectively**
    - **Both measures shown to be valid in prior studies**

# Background

- **A cut-off point at 12 months is usually recognized as a delayed TTP, reflecting impaired fertility**
- **In the general population, delayed TTP is observed in 10-15% of women of reproductive age**
- **Until now, no one has assessed if women with SLE had a delayed TTP**

# Objectives

- **We aimed to:**
  - **Measure TTP in women with SLE of reproductive age**
  - **Compare the occurrence of delayed TTP (i.e.  $\geq 12$  months) to general population figures**

# Methods

- **Women, aged 18-45 y, with SLE from the MGH lupus clinic enrolled between 2012 and 2017**
- **SLE diagnosed in accordance with the ACR classification criteria for SLE,**
- **At baseline and annual FU visit, the investigator administered a detailed reproductive questionnaire, wherein the TTP was measured**
- **TTP assessed :**
  - **Prospectively: for all pregnancies occurring over the follow-up period.**
  - **Retrospectively: for all pregnancies occurring prior to the baseline visit <2012**

# Methods

- **For pregnancies prospectively evaluated, we also measured:**
  - **SLICC damage index (SDI) score**
  - **Mean SLEDAI score over a maximum of 5 years**
  - **Anti-ovarian antibodies**
  - **Anti-Mullerian hormone (AMH)**
  - **Menstrual cycle irregularities**
  - **Previous cyclophosphamide (i.e. ever/never) and other relevant drug exposures (e.g. NSAIDs, steroids)**

# Results

- **A total of 333 women with SLE and aged 18-45 years completed the questionnaire**
- **Among these women, 135 never had a pregnancy and 198 conceived at least once**
- **In women having  $\geq 1$  pregnancies, we identified 400 pregnancies for which the TTP was assessed**

# Results

- **The TTP was measured retrospectively in 347 pregnancies, of which 226 and 121 respectively occurred prior and after SLE diagnosis**
- **We observed a TTP  $\geq 12$  months in:**
  - **4.9% (95% CI 2.6, 8.8) of pregnancies prior to SLE diagnosis**
  - **9.1% (95% CI 4.9, 16.0) of pregnancies after SLE diagnosis**

# Results

- **43 pregnancies occurred over the study period and 11.6% (95% CI 4.4, 25.9) had a TTP  $\geq$ 12 months**
- **They tended to be slightly older (median 33 vs 31 years)**
- **None of the women with prolonged TTP had prior cyclophosphamide exposure nor were exposed to steroids while attempting to conceive**
- **More likely to have a SDI  $\geq$ 1 [60% (95% CI 17, 92) vs 28% (95% CI 14, 47)] vs women with TTP < 12 months**

# Results

- **Table 2. Characteristics of pregnancies prospectively assessed (n=43)**

Variables	Pregnancies with TTP ≥12 months	Pregnancies with TTP <12 months
	(n=5)	(n=38)
Age, Median	33	31
SDI ≥1, n (%)	3 (60)	3 (60)
Cyclophosphamide, n (%)	0 (0)	0 (0)
Corticosteroids, n (%)	0 (0)	1 (3)
NSAIDs, n (%)	0 (0)	1 (3)
Irregular cycles, n (%)	1 (25)	0 (0)
Anti-ovarian ab, n (%)	1 (20)	3 (8)

# Discussion

- **First study to measure TTP in SLE pregnancies**
- **Our findings suggest that the occurrence of delayed TTP after SLE diagnosis is approximately 10%, similar to that of the general population**
- **The difference in number of women with delayed TTP prior and after SLE diagnosis might be accounted by age**
  - **Need to be further explored**

# Discussion

- **Almost half of women included have never been pregnant, of whom 89% never tried to conceive**
- **Might reflect disease-related psychosocial factors**

# Discussion

- **Potential limitations:**
  - **Few missing data**
    - **TTP unknown only for 49/449 (11%) pregnancies**
  - **Further analyses need to be done in relation to age, mean SLEDAI and AMH**

# Conclusion

- **Our findings suggest that the occurrence of delayed TTP after SLE diagnosis is similar to that of the general population, which has been consistently reported at approximately 10%**
- **However, larger observational studies, including notably an unexposed group of women without SLE, are needed to confirm our results**

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