# LUPUS NEPHRITIS AND PREGNANCY: MATERNAL AND FETAL OUTCOMES, RENAL RISK FACTORS, THERAPEUTIC PERSPECTIVES

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## INTRODUCTION AND AIMS

Sistemic Lupus Erythematosus (SLE) predominantly affects women, especially during fertile ages [1-2]. Lupus Nephritis (LN) was considered one of the major risk factors for maternal and fetal complications during pregnancy. Nephritis is often associated with hypertension, nephrotic syndrome, and decrease of renal function, all of which negatively affect the outcome of pregnancy[3]. Active lupus nephritis seems to increase the risk of premature birth and hypertension, while a history of nephritis is associated with higher rates of preeclampsia [4]. A modern management of this issue includes: evolution of immune-suppression, pre-conceptional counselling, achievement of inactive disease at conception, actuation of a local management protocol by a multidisciplinary teamwork in a tertiary care centre.The aim of our study is to compare pregnancies of women with SLE/LN and pregnancies in women with SLE, without LN, to evaluate the role of LN on the maternal and fetal outcome. We have also sought to identify renal risk factors for preeclampsia, preterm delivery before 34th week of gestation and IUGR below the tenth percentile.

## METHODS

A retrospective study was conduct on 99 pregnancies in 88 women with SLE, since 2003 to 2011 (demographics and clinical characteristics are reported in tables 1 and 2). All women are managed by a multidisciplinary team, including maternal-fetal-medicine obstetrician, rheumatologist, immunologist and nephrologist. During pregnancy we have implemented a protocol of intensive monitoring as showed in figure 1.

Tab. 1

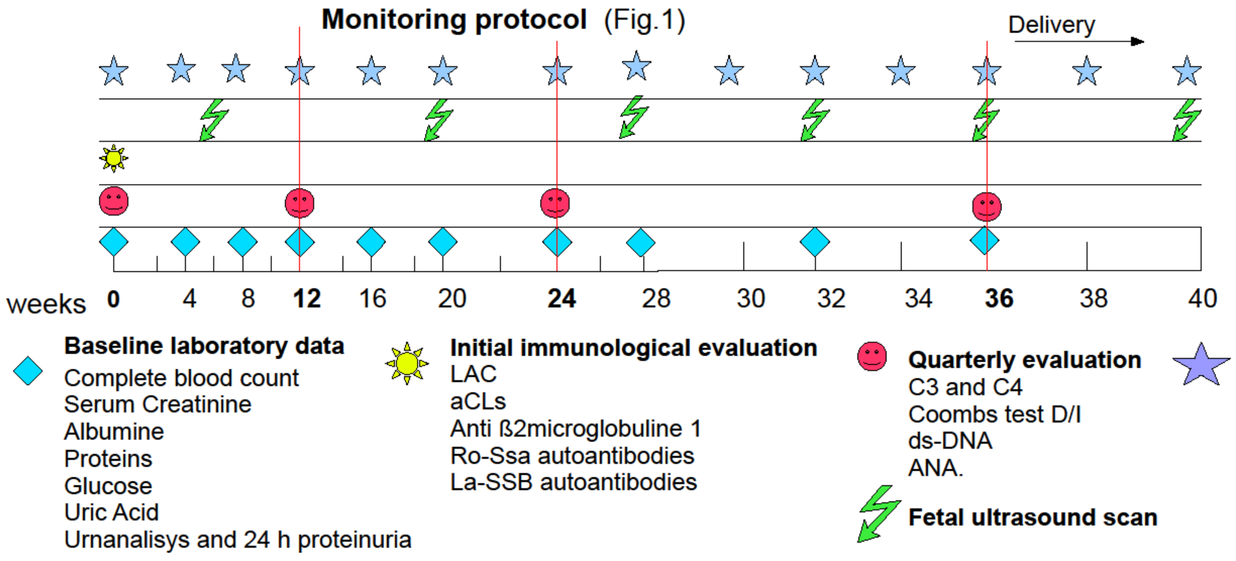
| Demographics characteristics | SLE/LN | SLE without LN |
|---|---|---|
| Women n° | 25 | 63 |
| Pregnancies n° | 29 | 70 |
| Pregnancies enrolled n° | 27 | 59 |
| Maternal age (mean±SD) | 32,1±4,7 | 34,1±5,23 |
| BMI (mean±SD) | 26,4 (17,03-28,17) | 22,8 (17,97-29,70) |
| Ethnicity n° (%)<br>-caucasian<br>-asian<br>-spanish | <br>29/29 (100%)<br>-<br>- | <br>68/70 (97%)<br>1 (1,5%)<br>1 (1,5%) |
| Nulliparous n° (%) | 20 (68,9%) | 40 (57,1%) |

Tab. 2

| Clinical characteristics | SLE/LN | SLE without LN |
|---|---|---|
| Years since SLE diagnosed (mean ±SD) | 8,3±14 | 5,7±4,6 |
| Prepregnancy S.Creatinine mg/dl (mean±SD) | 0,94±0,49 | 0,61±0,09 |
| Proteinuria at conception n° (%) | 18 (66,6%) | 2 (3,3%) |
| Chronic hypertension n°(%) | 10 (37%) | 6 (10,1%) |
| Active disease n° (%) | 3 (11,1%) | 8 (13,5%) |
| aPL positives n°(%) | 12 (35,5%) | 21 (44,4%) |
| APS n°(%) | 4 (14,8%) | 4 (6,7%) |
| aPL+APS n°(%) | 16 (59,2%) | 25 (42,3%) |

We divided our cohort into two groups of SLE pregnants: one with and one without renal involvement. 60,4% of woman received an antithrombotic prophylaxis in addition to immunosuppressive/ steroid drugs.(tab 3).
Low Molecular Weight Heparin was used in women with aPL, LMWH and Low Dose Aspirin in women with APS and LDA in women with lupus nephritis, altough aPL negative.(tab 4).Data were analyzed by a multivariate logistic regression.

**Monitoring protocol** (Fig.1)




Tab. 3

| Therapy | SLE/LN | SLE without LN |
|---|---|---|
| LMWH | 12(44%) | 21(34%) |
| LDA | 11(40%) | - |
| LDA+LMWH | 4(15%) | 4(6,7%) |
| Steroids | 21(77%) | 32(54%) |
| Immunosuppressive<br>-azathioprine<br>-chloroquine<br>-cyclosporine | <br>-<br>4(15%)<br>- | <br>1(1,7%)<br>10(17%)<br>1(1,7%) |

Tab. 4

| *Prophylaxis protocol* | *Drug* | N° women |
|---|---|---|
| aPL positives | LMWH | 33 |
| APS | LMWH + LDA | 8 |
| Lupus Nephritis (aPL negatives) | LDA | 11 |

## RESULTS AND CONCLUSIONS

The results showed that aren't significant differences in terms of pregnancy-outcome between nephropatics women and not, except for the incidence of renal flare, greater in nephropatics women (tab 5).Our cohort resulted almost homogeneus for demographics and clinical characteristics. There were no differences between the two groups for fetal outcome (tab 6).Risk factors for maternal and fetal complications are: decreased renal function at conception and pre-existing chronic hypertension.
Thrombophilia and nephropathy were not risk factors for maternal and fetal adverse events (tab 7).

Tab. 5

| PREGNANCY OUTCOME | SLE/LN n 27 | SLE without LN n 59 |
|---|---|---|
| Thromboembolic events n° (%) | 0 | 0 |
| Flare n° (%) | 9(33,3%) | 12(20,3%) |
| Renal Flare n°(%) | 5(18,5%) | 2(3,3%) |
| Preeclampsia/hellp n°(%) | 4(14,8%) | 4(6,78%) |
| Cesarean birth, n° (%) | 15(55,5%) | 29(49%) |
| Preterm delivery (<34 weeks), n° (%) | 4(14,8%) | 4(6,78%) |

Tab. 6

| FETAL OUTCOME | SLE/LN | SLE without LN |
|---|---|---|
| Live birth, n° | 27 | 59 |
| Perinatal death, n° | 1(25 weeks) | 1(25 weeks) |
| Gestational age at delivery (mean±SD) | 37±3,50 | 37,7±2,82 |
| Preterm delivery (<34 weeks), n°(%) | 4(14,8%) | 4(6,78%) |
| Mean birth weight, g, (mean±SD) | 2560±758 | 2878±743 |
| Weight Centile (mean±SD) | 35±27 | 43±29 |
| IUGR<10°centile, n° (%) | 5(18,5%) | 6(10,1%) |
| APGAR <7at 1° min | 1(2 ND) | 2(3ND) |

Tab. 7

| Outcome | OR | Std Err | z | P>z | IC 95% |
|---|---|---|---|---|---|
| Trombophilia | 0,34 | 0,18 | -1,99 | 0,05 | 0,12 0,98 |
| Nephropathy | 0,38 | 0,23 | -1,61 | 0,11 | 0,12 1,23 |
| Hypertension | 2,75 | 1,33 | 2,1 | 0,04 | 1,07 7,09 |
| Proteinuria | 2,45 | 1,5 | 1,46 | 0,14 | 0,74 8,16 |
| Serum Creatinine >1,2mg/dl | 1,25 | 0,45 | 0,63 | 0,53 | 0,62 2,53 |
| Quiescence | 0,87 | 0,39 | -0,32 | 0,75 | 0,36 2,11 |
| eGFR <90ml/min | 18,73 | 13,96 | 3,93 | 0 | 4,35 80,70 |

Our study shows that, with a modern model of treatment, pregnancy in patients with LN can be completed successfully, thanks to a multi-disciplinary approach in specialized centers, with the preconception assessment of the relative risk and trought adequate prophylaxis of adverse events.

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