criteria. The incidences of RA, PsA and PMR seem to be similar to those reported in previous study¹⁻³.

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FRI0704 ANALYSIS OF RISK FACTOR FOR PREGNANCY OUTCOMES IN 142 PREGNANCIES COMPLICATED WITH CONNECTIVE TISSUE DISEASE

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Background: Recently, many connective tissue disease (CTD) patients wish to become a mother because immunosuppressants and biologics enable to improve the outcome of underlying CTD and quality of life respectively. However, Pregnancies in CTD patients often have problems including underlying disease exacerbation, some complications during pregnancy especially in preterm birth, light for date (LFD) and premature rupture of membrane (PROM). Previous study identified that high clinical activities with hypocomplementemia and positive anti-dsDNA antibody were at highest risk for pregnancy loss and preterm delivery in SLE¹. It is unclear whether these problems are associated with the activity of underlying CTD or immunosuppressant treatment.

Objectives: We examine the issue of pregnancy and delivery complicated with CTD by the analysis of the cases in our institution.

Methods: We investigated the risk factors of preterm birth, LFD (light for dates) and perinatal complication from exacerbation of underlying disease, anti SS-A antibody, antiphospholipid antibody, doses of corticosteroid, immunosuppressants or biologics before pregnancy in 142 cases which were delivered in our institution.

Results: In 23 among all cases underlying diseases were exacerbated, and these occurred more often in PM/DM (60%), MCTD (33.3%), RA (15.3%) and SLE (13.3%). In SLE, SS, MCTD and PM/DM, preterm births and LFD were closely related to disease exacerbation and dose of corticosteroid, pulse therapy, and these were extracted as risk factors for these perinatal complications. Preterm birth was also associated with low complement (CH50) and high titer of anti-dsDNA antibody, and LFD was associated with high titer of anti-dsDNA antibody before pregnancy. However, there was no significant association with these factors in threatened premature delivery and PROM. In RA, perinatal complications were not influenced by methotrexate and biologics before pregnancy. However, only LFD was related with doses of corticosteroid during pregnancy.

Conclusions: We extracted disease exacerbation and dose of corticosteroid, pulse therapy during pregnancy and also low complement, high titer of anti-double stranded DNA antibody before pregnancy as risk factors of pregnancy outcomes. In pregnancy complicated with CTD, we need to control the disease activity strictly, however, we should consider the increase or pulse therapy of corticosteroid carefully.

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FRI0705 PROGRESSION OF CHRONIC DAMAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS AFTER 5-YEAR FOLLOW-UP: DATA FROM A LARGE MONOCENTRIC COHORT

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Background: The prevention of chronic damage represents one of the most important target in the management of patients affected by Systemic Lupus Erythematosus (SLE). About 50% of patients develop chronic damage, especially in the early disease phase, due to disease activity, treatment adverse events and comorbidities. Longitudinal studies demonstrated a progressive increase of damage, evaluated by using SLICC Damage Index (SDI).

Objectives: Moving from these evidences, we aimed at evaluating the progression of chronic damage in a monocentric SLE cohort with at least 5-year follow-up and identifying the factors associated with damage progression.

Methods: We analyzed 658 SLE patients diagnosed according to the ACR 1997 revised criteria, referring to a dedicated outpatient clinic. For the present analysis, we evaluated only patients with a minimum follow-up of 5 years and at least one visit per year. Clinical and laboratory data were collected in a standardized, computerized and electronically-filled form, including demographics, past medical history, comorbidities and concomitant treatments. In all patients, chronic damage was determined by using SDI, with the evaluation of 12 organ systems. Disease activity was evaluated by SLEDAI-2K. Furthermore, we calculated the number of flares during the follow-up, defined as an increase in SLEDAI-2K score ≥ 4 from the previous visit, with a minimum interval of 2 months between visits.

Results: According with the inclusion criteria, we analyzed data deriving from 198 SLE patients (17 M/181 F, mean $\pm$ SD age 46.8 $\pm$ 12.1 years, mean $\pm$ SD disease duration 131 $\pm$ 99.7 months). At the first visit 60 patients (30.3%) showed SDI>0; in particular SDI=1 was identified in 65%, SDI=2 in 18.3%, SDI=3 in 10%, SDI=4 in 6.7%. At baseline, the presence of chronic damage was significantly associated with age ($P<0.0001$) and disease duration ($P=0.001$). After 5 years, we registered the progression of chronic damage in 69 patients (34.8%), with a significant increase of SDI values (baseline: median SDI 0.0, IQR 0-1; follow-up SDI: median 0 IQR 0-2, $P=0.009$). SDI progression resulted significantly more frequent in subjects with damage at baseline (55.0%) in comparison with free-damage patients (26.1%, $P=0.0001$, Fisher exact test). The progression of chronic damage was significantly associated with neuropsychiatric involvement ($P=0.01$), disease activity in terms of number of flares during the 5-year follow-up ($P=0.001$), concomitant anti-phospholipid syndrome ($P=0.02$) and arterial hypertension ($P=0.001$).

Conclusions: In our study, we observed a progression of chronic damage in almost 30% of SLE patients after 5 years. In particular, the presence of previous chronic damage seem to be a risk factor for new damage development. Moreover, the lack of disease control and the presence of comorbidities allows damage progression. Taken together, the results of this study underline the need of a better management of SLE patients in order to prevent damage accrual.

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FRI0706 HLA-DRB1 ALLELES ARE ASSOCIATED WITH MARKERS OF ENDOTHELIAL INJURY IN FIRST-DEGREE RELATIVES OF RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid arthritis (RA) patients experience higher cardiovascular disease (CVD) risk and CVD-related mortality. MHC class II HLA-DRB1 alleles, or the shared epitope (SE), has also been linked to endothelial dysfunction in RA patients. It is not known whether this association exists in individuals who are RA-free, but who are at higher risk due to being a first-degree relative (FDR) of an RA patient.

Objectives: To determine the association between HLA-DRB1 alleles (*0401, *0404, *0405, *0408) and markers of endothelial injury in FDRs of RA patients, a population free of RA and RA-related medications.

Methods: From the Studies of the Etiology of RA, SERA, (a multicenter prospective study of preclinical RA, started in 2002), 113 FDRs who had been positive for any of 5 RA-related autoantibodies (Abs): rheumatoid factor (RF), RF isotypes - IgM, IgG, IgA, or anti-cyclic citrullinated peptide (anti-CCP2) on at least one of their visits, and 100 FDRs who had never been Ab positive were selected, frequency matched on age, sex, and field center site. No FDR met the 1987 ACR Criteria or 2010 EULAR/ACR Criteria for RA. In cross-sectional testing of single samples from baseline, the following were measured: endothelial injury markers: soluble intracellular adhesion molecule-1 (sICAM), soluble vascular cell adhesion molecule-1 (sVCAM) and E-selectin; and high resolution HLA-DRB1 typing for the *0401, *0404, *0405, and *0408 alleles using real-time polymerase chain reaction. ANCOVA was used to evaluate associations between HLA-DRB1 alleles, sVCAM, sICAM, and E-selectin, adjusting for age, sex, race, body mass index (BMI), Ab status, ever smoking, and current statin use.

Results: Among 213 FDRs, age was 50 $\pm$ 18 yr, BMI was 27 $\pm$ 6, 75% were women, 83% were Caucasian, 35% ever smoked, 11% were currently taking statins, and 38% were SE positive. sVCAM was significantly higher by 135ng/mL in FDRs with the HLA-DRB1*0404 allele ($p=0.009$) compared to FDRs without the *0404 allele (Table 1). E-selectin was higher by 23ng/mL in FDRs with the HLA-DRB1*0405

Table 1. Differences in levels of endothelial injury markers by HLA-DRB1 alleles in FDRs of RA patients

	n (%)	ICAM (ng/mL)	p-value	VCAM (ng/mL)	p-value	E-selectin (ng/mL)	p-value
SE Positive	81 (38)	11.6 (8.8)	0.19	55.7 (32.5)	0.09	3.7 (2.2)	0.09
401	55 (26)	2.6 (10.0)	0.80	-14.1 (37.0)	0.70	0.4 (2.5)	0.86
404	23 (11)	21.1 (13.9)	0.13	135.4 (50.9)	0.009	6.4 (3.4)	0.06
405	2 (1)	55.1 (44.0)	0.21	186.0 (163.1)	0.26	22.9 (10.8)	0.03
408	6 (3)	-6.6 (25.4)	0.79	7.1 (94.1)	0.94	8.1 (6.2)	0.19

*n=213 (92 Ab+, 121 Ab-).