Methods: Pregnant SLE patients (diagnosis made according to ACR 1997 criteria) were included in the present study, conducted in the context of a joint rheumatology/gynecology multi-disciplinary team. For each patient we collected demographic information, medical history, treatments, disease activity (SLEDAI-2K) chronic damage (SLICC *damage index*), clinical and laboratory data, including serum complement level and autoantibodies. Pregnancy outcomes were reported longitudinally as well as disease relapses occurring during pregnancy and puerperium. Flares were defined as new onset or worsening disease-related manifestation in any organ/system.

Results: Since 2008, 70 consecutive pregnancies occurred in 50 SLE patients [(median age at diagnosis 25 years (IQR 12.2), median age at first pregnancy 33 years (IQR 7), median disease duration 72 months (IQR 120)]. As controls, we evaluated 100 consecutive pregnancies in 100 women without autoimmune diseases [(median age 31 years (IQR 9)]. Table 1 reports the obstetric, fetal and neonatal outcomes of SLE patients compared to control group. A positive outcome in terms of live born infants was experienced in 88.6% of SLE pregnancies and in 88% of control group ($p=NS$). There were no statistically significant differences in any of the pregnancy outcomes evaluated; however, the percentage of small for gestational ages (SGA) was significantly higher in SLE group (22.8% *versus* 11.0% $P=0.003$). A statistical association was found between SGA and positivity for anti-dsDNA, anti-SSA and anti-SSB ($p=0.0001$, $p=0.01$, $p=0.04$ respectively). Miscarriage was significantly associated with disease-related serologic abnormalities [anti-dsDNA ($p=0.0001$), low C3 ($p=0.0001$) and low C4 ($p=0.006$)] and past smoking *habitus* ($p=0.0001$); preterm birth was associated with anti-dsDNA, anti-CL and anti-B2GPI ($p=0.001$, $p=0.0005$, $p=0.01$ respectively). A disease flare was reported in 28 pregnancies (40%) and in 31 puerperium (44.3%). Figure 1 reports SLE relapses divided according to organ involvement. Flare during pregnancy was associated with positivity for anti-SSA ($p=0.001$), anti-SSB ($p=0.01$) and a-CL ($p=0.006$), while *puerperium* relapses were associated with previous renal involvement ($p=0.0005$), flare during pregnancy ($p=0.01$) and chronic damage ($p=0.0001$).

Table 1. Pregnancy outcomes in 50 SLE and 100 controls.

	LES (Pregnancies N=70)	Controls (Pregnancies N=100)	P
OBSTETRIC OUTCOME			
Preterm birth N/%	18/25.7	19/19	NS
Gestational hypertension N/%	5/7.1	3/3	NS
Gestational diabetes N/%	5/7.1	5/5	NS
Pre-eclampsia N/%	2/2.9	1/1	NS
FETAL OUTCOME			
Miscarriages N/%	8/11.4	12/12	NS
PR interval elongation N/%	4/6.4	—	—
IUGR N/%	3/5	1/1	NS
NEONATAL OUTCOME			
SGA < 10 th centile N/%	16/22.8	11/11	0.003
Weight at birth median-I.Q.R.	2850-688	3250-814	0.003
Apgar 1' median-I.Q.R.	8-1	8-1	NS
Apgar 5' median-I.Q.R.	9-1	10-1	NS

Figure 1. Disease flares during and after 70 SLE pregnancies divided according to organ involvement.

Conclusion: The present study confirms the role of pre-gestational counseling and a multi-disciplinary approach in the outcome of SLE pregnancies. Moreover, the high prevalence of disease relapse even more justifies the need for a combined rheumatology/gynecology multi-disciplinary approach.

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SAT0229

PROTEOMIC ANALYSIS REVEALS ASSOCIATION BETWEEN IMMUNE-METABOLIC BIOMARKERS AND CLINICAL SYMPTOMS IN SICCA PATIENTS

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Background: Sjögren's syndrome (SS) is a systemic autoimmune disease whose main characteristic is involvement of the exocrine glandular system. Thus, its most common clinical manifestation is eye and mouth dryness which, alongside fatigue and pain, contributes to poor health-related quality of life (HRQoL). A growing body of evidence recognises the adipose tissue as an active endocrine organ secreting bioactive mediators involved in metabolic and inflammatory disorders. A relationship between obesity and symptoms in SS has not yet been elucidated.

Objectives: To explore potential associations between obesity-related immune-metabolic biomarkers and clinical symptoms in SS and sicca patients.

Methods: Proteomics analysis of 184 cardio-immuno-metabolic proteins was assessed on sera from 53 SS (50 females (F), 3 males (M); mean age 54 years) and 60 sicca (56 F, 4M; mean age 57 years) patients. Participants were enrolled in the Birmingham Optimising Assessment in Sjögren's Syndrome (OASIS) cohort and examinations included the EULAR SS Patient Reported Index (ESSPRI), Schirmer's test, unstimulated whole saliva, minor labial salivary gland biopsy, Euro-QoL-5 dimension (EQ-5D) tool, immunological parameters, body mass index (BMI) and HbA1c. Participants with SS fulfilled 2016 ACR/EULAR criteria. Non-SS sicca patients were anti-Ro antibody negative, displayed objective oral and/or ocular dryness, and did not have a physician diagnosis for SS. Linear regression analysis and univariate models were performed to identify the key predictors of symptoms.

Results: HRQoL as measured as EQ-5D utility values, symptoms as assessed by ESSPRI, and BMI did not differ between the SS and sicca group. However, strong correlations between BMI (or fat or fat-free mass) and EQ-5D and ESSPRI scores were found in the sicca but not in the SS group. Among several proteins investigated, ADM, TNFRSF13B, FGF23, IL10RB, CD5, CD40, IL1RA, TNFRSF9, TNFRSF10A, TNFRSF11A, TRAILR2, BARL9, SPON2, ACE2, LEP, CD4, IL12B, SLAMF1, PD-L1 positively correlated with symptoms in the sicca group ($R \geq 0.3$; Holm's adjusted $P \leq 0.05$). Adrenomedullin (ADM) showed the strongest correlation with ESSPRI ($R = 0.56$; $P < 0.0001$); age ($R = 0.45$; $P = 0.0003$); BMI ($R = 0.43$, $P = 0.0008$); Ocular Surface Disease Index ($R = 0.32$, $P = 0.03$); EQ-5D utility value ($R = -0.45$, $P = 0.001$) and VAS patient ($R = -0.41$, $P = 0.008$). There was no association between ADM and gender, Schirmer's test, disease and symptom duration ($P > 0.05$). ADM was independently associated with ESSPRI scores in non-SS sicca patients when corrected for BMI, age, HbA1c, depression and anxiety scores. None of the above mentioned proteins correlated with clinical symptoms in the SS group.

Conclusion: The study suggests that obesity-related immune-metabolic factors may play a role in regulating the symptoms in non-SS sicca patients. ADM appears to be a strong independent predictor of symptoms in these patients but not in SS.

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SAT0230

MACROPHAGE ACTIVATION SYNDROME IN SLE AND SYSTEMIC ONSET JIA: SIMILAR OR DISSIMILAR

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Background: Macrophage activation syndrome (MAS) is a serious complication in rheumatic disease. Fever and hyperferritinemia are common in systemic onset JIA and cytopenias are common in SLE thus recognising MAS in them is a challenge.

Objectives: We compared clinical, laboratory parameters, various classification criteria for MAS, and its outcome in SLE and sJIA.

Methods: Clinical and laboratory data were extracted from clinician diagnosed cases of MAS with SLE/sJIA who were admitted between 2004-2018 at a tertiary care hospital. Percentage of patients satisfying Ravelli, International consensus, HLH 2004 and criteria proposed by Parodi et al¹ were calculated.

Results: Among 33 patients (18 females) with MAS 19 had SLE and 14 had sJIA. MAS was more likely to be the presenting manifestation of disease in SLE as compared to sJIA ($p < 0.05$). There were no differences in the clinical features among these two diseases. EBV and CMV were identified in 2 patients each as the trigger for MAS.

Patients with SLE had lower baseline TLC and platelet whereas patients with sJIA-MAS had significantly higher median CRP ($p = 0.002$), fall in TLC ($p = 0.012$) and delta ESR/CRP ratio ($p = 0.02$) and lower fibrinogen level ($p = 0.006$). Neutrophil to lymphocyte ratio, Ferritin/CRP ratio and number of patients with Ferritin/ESR > 80 were similar. Bone Marrow hemophagocytosis was seen in only in 21% of patients. Only 6/33 fulfilled HLH criteria but criteria meant for sJIA or SLE performed well for both diseases and majority of patients could be diagnosed using them. Treatment included steroids(100%), cyclosporine(30%), Tacrolimus(21%), cyclophosphamide(21%), etoposide(3%) and thalidomide(12%). Mortality was similar in both groups.

Table 1. Agreement amongst MAS/HLH criteria in SLE and sJIA MAS

SLE-MAS	HLH	Ravelli et al	Consensus	Parodi et al
HLH	4	4	4	4
Ravelli et al	4	19	19	18
Consensus	4	19	19	18
Parodi et al	4	18	18	18
sJIA-MAS	HLH	Ravelli et al	Consensus	Parodi et al
HLH	2	2	2	2
Ravelli et al	2	12	11	12
Consensus	2	11	12	12
Parodi et al	2	12	12	14

Table 2. Comparison with various other cohorts

	Minoia et al sJIA n (%)	Our study sJIA, n (%)	Our Study SLE, n (%)	SLE, n (%) Ai-Chun Liu et al	Juvenile SLE n (%) Parodi et al
Number	362	14	19	32	38
MAS as presenting feature (%)	80 (22)	4 (28)	12 (63)	NA	24 (63)
Most common mani- festation (%)	Fever (96)	Fever (100)	Fever (89)	Fever (96)	Fever (89)
Most common trigger	Disease activity 251 (72.3)	Disease activity 8 (57)	Disease activity 12 (63)	Disease activity 32 (96)	Disease activity 38 (100)
BM done	150 (60.7)	2 (25)	5 (41)	32 (100)	20 (52)
hemophagocytosis					
Mortality	28 (8)	2 (14)	2 (10.5)	4 (12.5)	4 (11.4)
Patients meeting JIA criteria %	NA	-	100	NA	100
Patients meeting HLH criteria %	NA	14	19	NA	66

Conclusion: MAS is more likely to be presenting manifestation in SLE compared to sJIA. Though lab parameters are significantly different in MAS associated with SLE & sJIA, criteria meant for MAS in sJIA or SLE MAS performed equally well in both diseases.

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SAT0231

MULTIDIRECTIONAL DYSFUNCTION OF THE IMMUNE RESPONSE IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a multi-organ immune-mediated disease characterised by autoimmunity. Dysfunction in immune tolerance towards allergens and protection from infections has less been studied. Human leukocyte antigen (HLA) genotype affects the risk of developing SLE. Little is known on the role of HLA in shaping SLE phenotype.

Objectives: To test for potential associations among active SLE, occurrence of infections and hypersensitivity reactions (HyR) at a clinical level and assess whether these events segregate with patients' HLA-DRB1 typing.

Methods: 224 patients with SLE were prospectively followed up over the course of 1267 consecutive visits with a median interval of five months between each visit. HyR occurring within one month before or after each visit and occurrence of at least one infection leading to antimicrobial treatment and/or absence from work in the interval between each visit were recorded. Disease activity was estimated through the systemic lupus erythematosus disease activity index 2000 (SLEDAI-2K). Remission was surrogated by the Lupus Low Disease Activity State (LLDAS). Demographics and general disease features including a previous history of allergy were retrospectively assessed. HLA-DRB1 genotype was obtained from 188 patients. Data are expressed as median [interquartile range], unless otherwise specified.

Results: Incidence rates for HyR and infections were 80/1000 person-years and 45/100 person-years. Culprit agents for HyR were drugs in 61% of cases, inhalants, food or other allergens in the remainder 42%. Most frequent sites for infections were the airways (55%), skin and mucosae (16%), the genital and/or urinary tracts (14%) and the gastrointestinal tract (7%). LLDAS was inversely associated with HyR ($\chi^2 = 20.912$; $p < 0.0001$) or infections ($\chi^2 = 8.234$; $p = 0.005$). Patients with a recent HyR had a shorter disease duration [9 [2-15] vs 13 [8-22] years; $p = 0.006$] and higher SLEDAI-2K scores [4 [3.5-11] vs 3 [2-4]; $p < 0.001$] compared to patients without recent HyR. HyR were more frequently observed close to recent infections ($\chi^2 = 15.509$; $p < 0.0001$). Patients with HLA-DRB1*11:01 ($n = 28/188$) had more frequently a history of allergy than patients with other HLA-DRB1 genotypes ($\chi^2 = 4.944$; $p = 0.035$). Among patients with at least four prospective visits, HLA-DRB1*11:01 carriers reported a recent infection more frequently (25% [13-40%] vs 14% [0-29%]; $p = 0.044$) and HLA-DRB1*07:01 carriers less frequently (0% [0-17%] vs 18% [11-33%]; $p = 0.026$) compared to patients with other HLA-DRB1 genotypes.

Conclusion: These data suggest that immune dysfunction in SLE not only affects tolerance to self antigens but also antimicrobial and allergic responses and that genetically determined HLA-restricted mechanisms of antigen presentation might influence the shape of this dysfunctional immune response in patients with SLE.

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