Objectives: Our objective here was to analyse a clinically well-phenotyped patients using a suite of immune assessments and identify inter-relationships between these features as well as subgroups of patients who may differ in response to therapy.

Methods: 143 SLE patients were evaluated for clinical phenotype using BILAG-2004, autoantibodies using radioimmunoprecipitation (IP, University of Bath), two interferon scores (IFN-Score-A and IFN-Score-B), flow cytometry for major circulating immune cell subsets, as well as the surface protein expression of tetherin on each subset, a cell-specific assay for IFN response.

Unsupervised hierarchical clustering was used to define autoantibody subgroups. IFN scores (reflected dCT) were compared between the groups using multivariate models. Other variables were compared using Kruskal-Wallis test with pairwise comparisons.

Results: Using IP, 141 patients could be divided into five subgroups: U1RNP/Sm+ only (n=23), Ro60+ only (n=8), U1RNP/Sm+Ro60+ (n=6), Ro60+Ro52+La+ (n=11), Ro52+ (n=16) and other ANA (n=77).

Antibody subgroups was strongly associated with IFN-Score-A ($F=4.39$, $p=0.001$). Expression was lowest for "other ANA", intermediate for single antibody groups, and highest with multiple positive antibodies. Multivariate linear regression, including interaction terms between antibody types, revealed that Ro60 and U1RNP/Sm were the independent predictors of IFN-Score-A level ($p=0.051$ and 0.009 respectively). There was no association between autoantibody status and IFN-Score-B ($F=0.973$, $p=0.438$).

In flow cytometry, the U1RNP/Sm group was notable for significantly lower numbers of CD4-T-cells and memory-B-cells. Memory -B-cells were also lower in antibody-positive groups compared to "other ANA". Tetherin expression was increased in antibody positive groups, but to a similar extent on most cell subsets. Memory B cell tetherin was significantly higher in the groups with multiple positive antibodies.

U1RNP/Sm+ was associated with renal involvement ($p=0.004$). Mucocutaneous involvement was greater in the Ro60+Ro52+La+ group ($p=0.037$).

Conclusion: This cohort revealed relationships between immune features. U1RNP/Sm antibody was notable for defining a group of patients with a cluster of immune abnormalities, including the greatest elevation of IFN activity, greater abnormalities on flow cytometry and clinical renal involvement. This was independent to the IFN-Score-B high status that predicts better clinical response to rituximab (presented elsewhere at this conference). Future work in MASTERPLANS will investigate the significance of these subgroups for response to therapy.

Table 1: Multivariate analysis of antibody status and IFN Score A

Predictor	Ab-Negative Score-A Mean(SD)	Ab-Positive Score-A Mean(SD)	Univariate OR (95% CI)	P	Multivariable OR (95% CI)	P
U1RNP/Sm	3.59 (2.89)	1.46 (1.53)	-2.4 (-2.7, -0.34)	0.012	-2.7 (-2.7, -0.4)	0.009
Ro60	3.75 (2.82)	1.83 (1.72)	-3.1 (-3.0, -0.83)	0.001	-2.0 (-2.7, 0.0)	0.051
La	3.39 (2.72)	1.51 (1.39)	-2.0 (-2.7, -0.4)	0.046	-0.35 (-2.7, 1.9)	0.73
Ro52	3.52 (2.80)	1.95 (1.53)	-2.1 (-2.9, -0.22)	0.023	-0.86 (-2.4, 0.9)	0.39
U1RNP+Ro60	N/A	N/A	N/A	N/A	0.05 (-2.1, 2.1)	0.67
Ro60+Ro52	N/A	N/A	N/A	N/A	0.27 (-1.3, 1.8)	0.21
Ro52+La	N/A	N/A	N/A	N/A	-0.41 (-10.5, 1.26)	0.12

*Note these are untransformed dCT values, so numerically higher values represent lower gene expression

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FR10219

CD4+CD25+FOXP3+ REGULATORY T CELLS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: THE NEGATIVE ASSOCIATION WITH DISEASE ACTIVITY, ACUTE COURSE, TRANSITIONAL B CELLS AND IGG LEVELS

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Background: CD4+ CD25+ Foxp3+ regulatory T (Treg) cells play a key role in maintaining peripheral tolerance and preventing autoimmune disease. Quantitative and/or qualitative deficiencies of Treg have been associated with immune disturbances in systemic lupus erythematosus (SLE).

Objectives: The main goal of the study was to determine the relationship of CD4+CD25+FoxP3+Treg cells with clinical and immunological manifestations in SLE patients (pts).

Methods: Frequencies and absolute numbers of peripheral blood CD4+CD25+FoxP3+Treg cells were assessed in 21 healthy donors and 20 SLE pts (2012 SLICC classification criteria); (1M/19F); age 32±13 years; disease duration median (25–75 percentile) 5(1–10) years; SLEDAI2K≥10 - 15(10–22) (14 pts), <10 - 7(6–8) (6 pts). All pts were treated with prednisone, hydroxychloroquine, azathioprine, mycophenolate mofetil, cyclophosphamide. CD4+CD25+FoxP3+ Treg cells and B-cell subsets were analyzed using multicolor flow cytometry.

Results: Compared with healthy donors, SLE pts demonstrated significant lower the absolute number of Tregs (0.05; 0.04–0.06 vs 0.03; 0.02–0.05×10⁹/L, $p<0.036$), with a high percentage of Treg (8.8; 7.5–10.5 vs 12.0; 8.8–17.0%, $p<0.02$). The median percentage of Tregs was lower in pts with acute SLE compared to chronic SLE pts (9.0; 8.3–9.9 vs 13.5; 12.7–18.7%, $p<0.02$). SLE pts with high activity had a lower frequencies of Tregs (10.2; 8.5–15.0 vs 15.8; 12.7–20.4%, $r=-0.51$, $p<0.05$). Low count of Tregs correlated with elevated level of IgG ($r=-0.52$, $p<0.05$). Absolute number of Tregscorrelated negatively with percentage and absolute count of transitional (CD19+IgD+CD10+CD38++CD27-) B cells ($r=-0.66$ and $r=-0.63$, $p<0.05$).

Conclusion: Decreased amount of T regs in SLE is associated with high disease activity, acute course and expansion of autoreactive B cells.

REFERENCES:

- [1] Zhang SX, Ma XW, Li YF, Lai NL, Huang ZH, Fan K, Wang CH, Li XF. The Proportion of Regulatory T Cells in Patients with Systemic Lupus Erythematosus: A Meta-Analysis. *J Immunol Res*. 2018 Sep 3;2018:7103219. doi: 10.1155/2018/7103219.
- [2] Żabińska M, Krajewska M, Kościńska-Kasprzak K, Jakuszek K, Bartoszek D, Myska M, Klinger M. CD4(+)CD25(+)CD127(-) and CD4(+)CD25(+)Foxp3(+) Regulatory T Cell Subsets in Mediating Autoimmune Reactivity in Systemic Lupus Erythematosus Patients. *Arch Immunol Ther Exp (Warsz)*. 2016 Oct;64(5):399–407. doi: 10.1007/s00005-016-0399-5.

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FR10220

OCULAR SURFACE INFLAMMATORY MARKERS CORRELATED WITH IMMUNOLOGICAL PARAMETERS IN PRIMARY SJÖGREN'S SYNDROME

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Background: In Sjögren's Syndrome (SS), ocular damage is mediated by inflammation induced by antibodies, enzymes, and other effectors that could be used as clinical indicators of the ocular surface damage. There is evidence suggesting that increased activity of matrix metalloproteinases (MMPs) is correlated with an increased ocular damage because of its potential inflammatory activity and could be used as a potential therapeutic target for dry eye^{1,2}. Very few studies have addressed the role between the ocular MMPs and the clinical parameters of SS.

Objectives: To determine the level of correlation between the serological profile of autoantibodies with ophthalmological parameters at the cornea level.

Methods: Cross-sectional, observational, and descriptive study. Sixty patients with a diagnosis of primary Sjögren's syndrome (pSS) classified according to the ACR/EULAR 2016 criteria were included. The following measurements were made: Schirmer test, lacrimal osmolarity, ocular staining score (OSS), and ocular surface disease index (OSDI) and metalloproteinase-9 (MMP-9) in tear and antibodies were measured in peripheral blood serum: RF isotypes (IgA, IgG, IgM), anti-SSA/Ro and anti-SSB/La in.

Results: Fifty-eight women participated (96.7%) with an average age of 53 years (± 13.01) (Table 1). We found a positive correlation between OSS and RF-IgM ($\rho=0.385$ $P=0.002$), RF-IgA ($\rho=0.256$ $P=0.049$), and anti-Ro/SSA ($\rho=0.302$ $P<0.019$). We found a statistically significant association between the seropositivity of the Anti-SSA/Ro antibody and the presence of MMP-9 in tears (OR 4.38, CI 95% 0.877–21.92, $P=0.057$). A

Spearman correlation test and the association between MMP9 and serology were evaluated with χ^2 test.

Table 1. Demographic characteristics in Hispanic patients with primary Sjögren's Syndrome

Age, median (DS)	53.23 (13.0)
Female, n (%)	58 (96.7)
Anti-Ro/SSA, n (%)	41 (68.3)
Anti-La/SSB, n (%)	18 (31.6)
RF IgG, n (%)	13 (21.7)
RF IgM, n (%)	31 (51.7)
RF IgA, n (%)	24 (40.0)
Schirmer, n (%)	38 (63.3)
OSDI, n (%)	52 (86.7)
OSS, n (%)	43 (71.7)
Metalloproteinase 9, n (%)	14 (23.3)
Ocular Osmolarity >300, n (%)	45 (75.0)
Abnormal USF, n (%)	45 (75.0)
GSMB, n (%)	51 (85.0)

RF: Rheumatoid Factor, OSDI: Ocular Surface Disease Index, OSS: Ocular Staining Score, USF: Unstimulated Salivary Flow; MSGB: Minor Salivary Gland Biopsy.

Conclusion: A significant correlation was observed between serology, ocular surface damage (OSS), and ocular surface inflammation (MMP-9). The positivity of RF isotypes IgM and IgA could alert the clinician about the ocular damage to initiate a study directed to this organ. Nevertheless this present study shows preliminary outcomes, we need to enroll more patients to obtain better outcomes.

REFERENCES:

- [1] Aluri, H. S., et al. (2015). Role of Matrix Metalloproteinases 2 and 9 in Lacrimal Gland Disease in Animal Models of Sjögren's Syndrome. *Investigative ophthalmology & visual science*, 56(9), 5218-28.
- [2] Messmer, E. M., et al. (2016). Matrix Metalloproteinase 9 Testing in Dry Eye Disease Using a Commercially Available Point-of-Care Immunoassay. *Ophthalmology*, 123(11), 2300-2308. <https://doi.org/10.1016/j.optha.2016.07.028>.

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FRI0221 CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME IN PREGNANCY: CASE SERIES

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Background: Catastrophic antiphospholipid syndrome (CAPS) is a rare condition associated with high mortality¹. Prompt recognition and treatment is important for optimal outcomes. Clinical features of CAPS can overlap with obstetric complications, leading to diagnostic challenge².

Objectives: Describe two patients with CAPS during immediate post-partum period.

Methods: We report two cases in a single centre over two years.

Results: A 38 year old with obstetric Antiphospholipid syndrome (APS) presented with epigastric pain, transaminitis and thrombocytopenia in keeping with evolving HELLP syndrome. Spontaneous complete miscarriage ensued. Post-delivery, she developed worsening abdominal pain and transaminitis (Table 1). Imaging demonstrated hepatic infarcts and patchy ground glass lung opacities. She was treated for CAPS with intravenous steroids and anticoagulation, and recovered.

A 39 year old with primary APS (deep venous thrombosis and obstetric features) whose antenatal course was fraught with minor per vaginal bleeding (PVB) presented with heavy PVB at 22 weeks gestation requiring cessation of anticoagulation. She developed a deep venous thrombosis. Risk of clot propagation versus bleeding prompted cautious anticoagulation. Labour was induced for declining maternal health and poor foetal prognosis at 24 weeks, 3 days. Post-delivery, she developed abdominal pain, headache, transaminitis and worsening thrombocytopenia with heavy PVB requiring uterine artery embolization. Given features that were consistent with micro thrombi and ischaemia (Table 1), she was treated as for CAPS and HELLP syndrome with intravenous steroids, plasma exchange (PLEX) and intravenous immunoglobulin (IVIG), and recovered.

Table 1

	Case 1	Case 2
Gestational age on admission	17 weeks 5 days	22 weeks 5 days
Treatment during pregnancy prior to CAPS	LMWH ¹ once daily, Aspirin	LMWH twice daily, Aspirin, Steroids, Hydroxychloroquine, monthly IVIG
Time of onset of CAPS	2 nd day after foetal loss	4 th day after foetal loss
Organ involvement	Hepatic, Pulmonary, Placenta	Hepatic, Central nervous system, Placenta
Laboratory results at onsets of CAPS		
Haemoglobin (g/dL)	7.4	10.1
Platelets (x10⁹/L)	82	28
AST²/ALT³/LDH⁴ (U/L)	137/140/690	1199/1130/2206
Estimated proteinuria (g/day)	2.7	2.3
Positive serologies	Anti-Ro Anti-nuclear antibody, Anti-double stranded DNA, Lupus anticoagulant, Anti-cardiolipin IgM/IgG, B2 glycoprotein IgM/IgG	
Treatment	IV MP ⁵ , LMWH 1mg/kg/day twice daily	IV MP, PLEX, IVIG, LMWH 1mg/kg/day twice daily
Outcomes		
Obstetric	Intra-uterine foetal demise	
Maternal	Recovery	

¹Low molecular weight heparin. ²Aspartate aminotransferase. ³Alanine aminotransferase. ⁴Lactate dehydrogenase. ⁵Intravenous Methylprednisolone

Conclusion: Recognition of CAPS is complex in pregnancy. Vigilance is required for urgent aggressive treatment to improve outcomes in this uncommon condition.

REFERENCES:

- [1] Bucciarelli S, Espinosa G, Cervera R, et al. Mortality in catastrophic antiphospholipid syndrome: causes of death and prognostic factors in a series of 250 patients. *Arthritis Rheum* 2006; 54: 2568-2576.
- [2] Silver RM. Catastrophic antiphospholipid syndrome and pregnancy. *Semin Perinatol*. 2018 Feb;42(1):26-32.

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FRI0222 ANALYSIS OF CLINICAL AND SEROLOGICAL PICTURE OF PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME AND AN EARLY DISEASE ONSET AT AGE BEFORE 35 YEARS

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Background: Primary Sjögren's Syndrome (pSS) is a chronic systemic autoimmune disease with diverse clinical picture, extending from exocrinopathy to systemic disease and non-Hodgkin's lymphoma (NHL). Usually, it affects middle aged women, but early disease onset (≤ 35 years old) has been also observed. So far, there is a limited number of studies to explore whether the age of SS onset affects the clinical SS phenotype¹. To definitely answer this question a well-organized, large, harmonized cohort of patients with a continuous follow up is needed, through the ongoing European project (HarmonicSS, grant agreement no: 731944).

Objectives: To investigate whether the clinical and serological picture of pSS patients with early disease onset (≤ 35 years old) differs to that of middle-age onset.

Methods: Medical records of 717 pSS patients, included in two Greek cohorts fulfilling the 2002 revised European/American International classification criteria for SS, were evaluated. The study group included 133 (18.5%) patients with disease onset ≤ 35 years (median disease duration, range: 10, 0-32 years; group A) matched at 1:1 ratio according to gender and disease duration with 133 pSS patients with middle-age onset (mean