examination and by chart review were correlated to the presence or not of aPL TP.

Results: Nineteen out of 74 pAPS patients had aPL TP (25.7%). Demographic and clinical characteristics are shown in Table 1. In a bivariate analysis, TP was associated with the presence of combined thrombotic and obstetric manifestations ($p=0.008$), three or more abortions (abortion 3+; $p=0.043$), and livedo ($p=0.023$). In a multivariate regression analysis, the model was adjusted to age, sex, race and variables with $p<0.10$ in the bivariate analysis (arterial thrombosis, abortion 3+, livedo, thrombocytopenia, and thrombotic+obstetric). After the analysis, arterial thrombosis (OR 5.74; CI95% 1.31–25.05; $p=0.02$) and abortion 3+ (OR 12.55; CI95% 1.01–156.54; $p=0.049$) were associated with TP.

Conclusions: In our cohort of primary APS patients, triple positivity was associated with arterial thromboses and the occurrence of 3 or more abortions, with increased risk over 5 and 12 folds, respectively.

Disclosure of Interest: None declared

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THU0254 COMPARISON OF URBAN VERSUS RURAL ENVIRONMENT ASSOCIATED SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): RISK AND CLINICAL FEATURES

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Background: SLE originates from the complex interplay between genetic, epigenetic and environmental factors but the effects of the latter remain elusive. Very few studies have examined the impact of the place of residence (urban/rural) on SLE clinical profile and outcomes.

Objectives: To evaluate the effect of rural versus urban place of residency with regards to: i) SLE occurrence; ii) delay in diagnosis; iii) clinical manifestations, severity and non-reversible organ damage; iv) comorbidities and hospitalizations.

Methods: We employed data from the Lupus Epidemiology & Surveillance project in Crete (750 adult SLE patients with ≥ 4 ACR-1997 classification criteria). Crete is a Mediterranean island with genetically stable and homogenous population in ethnicity and sociodemographic characteristics, with no significant inequalities regarding access to healthcare facilities; 61% of the inhabitants live in rural ($<10,000$ people) and 47% in urban areas ($>10,000$ people). Demographics and residency history were retrieved from face interviews. In 200 patients with exclusively urban or rural residence, a subanalysis was performed in relation to disease risk, diagnosis age, disease severity, renal and neuropsychiatric involvement, and organ damage (SLICC damage Index [SDI]).

Results: SLE prevalence (December 2013) varied across the four geographical prefectures of Crete (Figure 1) and was significantly higher in urban ($165/10^5$) than rural ($123/10^5$) areas ($p<0.001$). The relative risk of SLE in urban versus rural regions was 2.0 (95% Confidence Interval 1.5–2.9). Notably, patients in urban regions had lower age of diagnosis (38.0 ± 13.4 vs. 44.5 ± 14.8 years, $p=0.005$) and female-to-male ratio (6.5:1 vs. 11:1) than those in rural regions. Delay >2 years between symptoms onset and SLE diagnosis occurred in 42% of patients from rural areas as compared to 32% of those from urban areas ($p=0.01$). Acute cutaneous lupus was more prevalent in the rural environment (83.9% vs. 72.6%, $p=0.05$) whereas the opposite trend was noted for discoid rash (2.3% vs. 16.8%, $p=0.001$). Nephritis occurred less frequently (10.3% vs. 12.4%) and neuropsychiatric disease was more prevalent (14.9% vs. 10.6%) in rural than urban patients albeit non-significantly. Prevalence of mild, moderate, and severe disease was 42%, 40%, and 18% in patients from rural areas, the respective figures being 55%, 28% and 18% in those from urban areas ($p=0.12$). Hospitalization due to active lupus did not differ between the two groups. At last follow-up, 45.3% of the patients living in urban and 51.9% of patients in rural areas had no organ damage ($p=0.89$). Concurrent allergic diseases were more frequent in urban patients (30.9% vs. 14.3%, $p=0.045$), particularly allergic rhinitis (8.8% vs. 2.3%, $p=0.05$).

Conclusions: SLE may be more prevalent in urban than rural regions and urbanization is associated with increased risk of SLE and earlier age of disease onset.

Our results suggest an important effect of the environment on SLE occurrence and characteristics, which warrants further investigation.

Disclosure of Interest: None declared

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THU0255 COMPARISON OF REMISSION AND LUPUS LOW ACTIVITY STATE AS PREDICTORS OF ORGAN DAMAGE

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Background: Outcome measures that combine control of SLE activity and prednisone reduction are clinically relevant. A clinical goal in SLE is to reduce risk of long-term organ damage.

Objectives: We assessed whether two recently proposed disease activity outcomes were predictive of future damage.

Methods: For each month of follow-up in a large SLE cohort, we determined whether the patient was in Clinical Remission (as defined by the DORIS work group) or low lupus disease activity state (LLDAS) (as defined by Franklyn et al.). Clinical Remission was defined as a PGA <0.5 , clinical SLEDAI=0 and no prednisone or immunosuppressants. Clinical Remission on Treatment allowed for prednisone ≤ 5 mg/day and immunosuppressant use. LLDAS was defined as a SLEDAI ≤ 4 , PGA ≤ 1.0 , no major organ activity, and no new activity. LLDAS on treatment allowed for prednisone use ≤ 7.5 mg/d and immunosuppressants. Damage was defined using the SLICC/ACR index.

Results: There were 81,118 person-months observed among 2,026 patients (92% female, 53% Caucasian, 39% African-American). Table 1 shows the rates of damage, per person month, in subgroups defined by Remission or LLDAS.

Table 1. Rates of new damage, in subgroups defined by past levels of disease activity

Percentage of prior months in:	Number of person-months observed	Number of months with an increase in SLICC/ACR damage	Rate of damage per 100 person-months	Rate ratios	P-values
Clinical Remission					
None	35,772	406	1.13	1.0 (Ref)	
Not none, but $<25\%$	14,358	102	0.71	0.60 (0.48, 0.75)	<0.0001
25% to 50%	6573	50	0.76	0.66 (0.46, 0.94)	0.023
50% to 75%	3845	27	0.70	0.63 (0.42, 0.97)	0.035
75%+	1,641	10	0.61	0.58 (0.30, 1.15)	0.12
Clinical Remission on Treatment					
None	16,491	250	1.52	1.0 (Ref)	
Not none, but $<25\%$	20,169	170	0.84	0.54 (0.44, 0.67)	<0.0001
25% to 50%	14,344	103	0.72	0.46 (0.36, 0.60)	<0.0001
50% to 75%	8396	54	0.64	0.43 (0.30, 0.60)	<0.0001
75%+	2,789	18	0.65	0.45 (0.27, 0.75)	0.0019
LLDAS					
None	30,366	343	1.13	1.0 (Ref)	
Not none, but $<25\%$	10,880	106	0.97	0.86 (0.69, 1.07)	0.18
25% to 50%	5012	40	0.80	0.70 (0.51, 0.98)	0.037
50% to 75%	8494	60	0.71	0.63 (0.48, 0.83)	
75%+	7,527	46	0.61	0.54 (0.40, 0.73)	<0.0001
LLDAS on Treatment					
None	7,656	117	1.53	1.0 (Ref)	
Not none, but $<25\%$	10,555	134	1.27	0.83 (0.65, 1.06)	0.14
25% to 50%	12,686	129	1.02	0.66 (0.51, 0.85)	0.0013
50% to 75%	18,151	133	0.73	0.48 (0.37, 0.61)	0.0010
75%+	13,141	82	0.62	0.40 (0.30, 0.54)	<0.0001

Damage rates were relatively low when LLDAS was achieved at least 50% of the time. These rates were similar to those experienced by patients who met a more stringent treatment restriction with Remission on Treatment at least 50% of the time.

Conclusions: The equivalence of LLDAS and DORIS remission on treatment is welcome news, as LLDAS on treatment $>50\%$ of the time is an easier goal to achieve (3 times more person-months observed in our cohort) and more realistic as a clinical trial outcome.

Disclosure of Interest: None declared

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THU0256 DEVELOPMENT AND VALIDATION OF A SCORE TO PREDICT THE RISK OF SEVERE INFECTION IN SLE

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Background: Infection is a major cause of morbidity and mortality in SLE patients. It would be helpful to have a tool to predict the risk that an individual patient with SLE will develop serious infection.

Objectives: To develop a predictive risk calculator algorithm (SCORE) that

assesses the probability of serious infection (i.e. leading to hospitalization) in SLE patients and to test it in an independent cohort.

Methods: The SCORE was developed using data from the RELESSER (Spanish Society of Rheumatology Lupus Registry) cohort of 3658 SLE patients. A Cox regression model for repeated events (Andersen-Gill) was applied to assess which demographic and clinical factors were independently associated with increased risk of developing serious infection (Table 1). The SCORE was then validated using retrospective data from the UCLH (University College London Hospital) cohort including 699 SLE patients. Median SCORE values were compared between sub-groups of patients using the U-Mann-Whitney test.

Results: Among 699 SLE UCLH patients, 98 (14%) developed serious infection. We compared these patients with 111 SLE controls who have never suffered serious infection. The characteristics of both groups are summarized in table 2. The infection group were more likely to have suffered previous infection ($P=0.001$) and/or hospitalized for SLE ($P<0.001$) and had renal and joint disease ($P=0.005$). Over a quarter of the infection group died from their infection. Median (Md) SCORE at diagnosis in SLE patients with infection was 4.27 (IQR 3.18) which was significantly higher than in the control group (Md 2.55, IQR 3.79) ($z=3.341$; $P=0.0008$). Md SCORE before infection in patients was 5.3 (IQR 3.68) which was significantly higher than SCORE at diagnosis ($z=-5.733$; $P<0.001$) in those patients. By ROC analysis, we defined three possible cut-offs to distinguish patients with and without infection. The area under the ROC curve was 0.66 (CI 95% 0.56 to 0.71). A cut-off for SCORE at diagnosis >3.18 identified patients who would develop serious infection with sensitivity (S) 76.5% and specificity (SPC) 50.5%. For SCORE >3.79 , S was 64.3% and SPC 57.7%. For SCORE >4.24 , S was 64.3% and SPC 60.4%.

TABLE 1 – FACTORS INCLUDED IN THE “SCORE”

Risk factor	B	P-value	HR
Age at diagnosis (>46 years old)	0.1163	0.001	1.12
Latin American ethnicity	0.427	0.001	2.40
Corticosteroids (>10 mg/day) at time of calculating SCORE	0.2878	0.001	1.33
Sex=male	0.3692	0.0001	1.49
Previous hospitalization (for SLE)	1.0049	<0.00001	2.73
Katz index	0.062	0.002	1.06
Prior infection at any time	0.8739	<0.0001	2.40

Table 2

	SLE-infection (n=98)	SLE-non infection (n=111)	P value
Gender	Females: 90 (91.8) Males: 8 (8.2%)	Females: 103 (92.8%) Males: 8 (7.2%)	ns
Mean age (diagnosis of SLE)	30.5 (27)	31 (18)	ns
Ethnicity	Caucasian 48 (49%) Latin American 3 (3.06%) African/Caribbean 28 (28.6%) Asian 7 (7.1%) Other 12 (12.2%)	Caucasian 72 (64.9%) Latin American 2 (1.8%) African/Caribbean 20 (18.02%) Asian 6 (5.4%) Other 12 (10.8%)	ns
Median length of follow-up (IQR)	9.5 (14) yrs	14 (9) yrs	0.001
Previous treatment	Steroids (at any time) 89 (90.8%) MMF 25 (25.5%) AZA 46 (47%) Cyclophosphamide 20 (20.4%) Biological treatment 24 (24.5%)	Steroids (at any time) 61 (55%) MMF 23 (20.7%) AZA 29 (26.1%) Cyclophosphamide 13 (11.7%) Biological treatment 22 (19.8%)	<0.001 ns <0.001 0.01 ns
Patients with >1 Infection	18 (18.4%)		

Conclusions: We have developed a SCORE for predicting risk of serious infection in SLE and validated it in an independent cohort. Given the potential mortality from such infections, this SCORE could be clinically useful though the moderate sensitivity and specificity necessitate caution and further prospective studies.

Disclosure of Interest: None declared

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THU0257 ENHANCED ACTIVATION OF NLRP3 INFLAMMASOMES IN PATIENTS WITH SJÖGREN'S SYNDROME

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Background: There has been data about pathogenic role of NLRP3 inflammasome in Sjögren's syndrome. However, linkage between their clinical features and NLRP3 inflammasome has not been clearly defined.

Objectives: The aim of this study is to identify the association of NLRP3 inflammasome with clinical features in patients with primary Sjögren's syndrome.

Methods: A total 25 female patients with Sjögren's syndrome and gender-matched 25 healthy controls were consecutively enrolled. The mRNA expression for target genes including NLRP3, ASC, caspase-1, IL-1b, and IL-18 in peripheral blood mononuclear cells (PBMCs) were measured using real-time polymerase chain reaction. Serum IL-1b and IL-18 expression were also measured by ELISA method. Clinical information and disease activity and damage for Sjögren's syndrome such as EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) and Sjögren's Syndrome Disease Damage Index (SSDDI) were collected at the time of enrollment. Statistical analysis were applied including Spearman's correlation coefficient and Mann-Whitney t-test.

Results: Patients with Sjögren's syndrome was found to be highly expressed in mRNA IL-1b and its protein, compared to controls ($p<0.001$ and $p=0.001$, respectively). The mRNA levels of caspase-1 and ASC were significantly higher than those in controls ($p=0.021$ and $p=0.008$, respectively), but not mRNA level of NLRP3. The mRNA level of IL-1b is closely related with mRNA level of NLRP3 and ESR ($r=0.549$, $p<0.001$ and $r=0.577$, $p=0.003$, respectively). Serum IL-1b protein expression in Sjögren's syndrome was found to be associated with mRNA level of caspase-1. Based on SSDDI, patients with SSDDI ≥ 1 was older and higher IL-1b and NLRP3 mRNA expression, compared to those with SSDDI = 0 ($p=0.035$, $p=0.005$, and $p=0.016$, respectively).

Conclusions: This study confirmed that activation of NLRP3 inflammasome might implicated the pathogenesis of Sjögren's syndrome.

Disclosure of Interest: None declared

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THU0258 SERUM PARAOXONASE 3 LEVELS ARE DECREASED AND PARAOXONASE 3 ACTIVITY IS REDUCED IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AS COMPARED TO HEALTHY CONTROLS

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Background: Premature atherosclerosis is a well recognised comorbidity in patients with SLE (1). Elevated levels of circulating Oxidised Low Density Lipoprotein (OxLDL) have been described in SLE patients, especially in those with a history of cardiovascular disease (2). Paraoxonase 3 (PON 3) is believed to play a role in prevention of atherosclerosis by contributing towards the anti oxidant actions of high density lipoprotein (HDL).

Objectives: To determine serum PON3 levels and PON 3 activity in patients with SLE and compare them with healthy controls.

Methods: Serum PON 3 levels and PON3 activity were determined in 100 patients of SLE with no prior history of coronary artery disease and they were compared with those of 50 healthy controls who did not have diabetes, hypertension or coronary artery disease. Serum PON3 concentration was determined by enzyme-linked immunosorbent assay (ELISA) using anti-PON3 antibody specific for human PON3. PON 3 activity was estimated using Spectrophotometric assay which quantified the hydrolysis of dihydrocoumarin at 270 nm (3).

Results: PON 3 levels were lower in SLE patients ($P<0.001$) and PON 3 activity was reduced ($p<0.001$) as compared to healthy controls. In subgroup analysis of SLE patients, PON 3 activity and levels did not correlate with disease activity. On Univariate analysis, serum creatinine ($r^2=0.06$, $p<0.002$), age ($r^2=0.03$, $p=0.035$), and SLE status ($r^2=0.27$, $p<0.001$) contributed to PON3 levels. On Univariate analysis, serum creatinine ($r^2=0.15$, $p<0.001$), AST ($r^2=0.04$, $p=0.01$), ALT ($r^2=0.16$, $p<0.001$) and SLE status ($r^2=0.77$, $p<0.001$) contributed to PON3 levels. On multivariate analysis, only SLE status predicted PON 3 levels ($P<0.001$) and PON 3 activity ($p<0.001$).

Parameter	SLE patients	Healthy controls	P value
Serum Creatinine (mg/dl)	0.55 (0.19)	0.58 (0.19)	<0.001
Aspartate aminotransferase (U/L)	22 (11)	21 (18)	0.02
Alanine aminotransferase (U/L)	12.45 (13)	26.5 (15)	<0.001
Alkaline Phosphatase (U/L)	70 (34)	63.5 (49)	0.408
Total cholesterol (mg/dl)	155 (67)	168.5 (25)	0.076
Low density lipoprotein (mg/dl)	84.5 (44)	102 (28)	0.023
High density lipoprotein (mg/dl)	41 (21)	43 (11)	0.329
Triglyceride (mg/dl)	136 (96)	129 (64)	0.359
Very low density lipoprotein (mg/dl)	27 (19)	26 (12)	0.344
Paraoxonase 3 activity*	38.43 (37.64)	69.54 (27.80)	<0.001
Paraoxonase 3 levels**	0.54 (0.32)	2.41 (1.06)	<0.001

All values are in Median (Interquartile Range). * $\mu\text{mol ml}^{-1} \text{ min}^{-1}$, ** $\mu\text{g ml}^{-1}$.

Conclusions: PON3 levels are reduced and PON 3 activity is decreased in patients with SLE as compared to healthy controls, the difference was attributable to the disease itself. This may contribute to premature atherosclerosis in these patients.

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