Assessment (PGA) (0-3 points, 10 cm scale), SLEDAI-2K and SLE-DAS. A senior rheumatologist expert in SLE, blinded to the disease activity scores, classified each patient in 1 of 4 categories: (i) remission, (ii) low disease activity (LDA), (iii) mild disease activity and (iv) moderate/severe disease activity. The best cut-off values of SLE-DAS to define these categories were estimated using Receiver Operating Characteristic (ROC) curve analysis. Accuracy, precision, sensitivity and specificity values for these cut-off values were then calculated. The agreement between the SLE-DAS and physician's classification was measured using Kappa coefficient. Statistical significance was set at 0.05.

Results: We included 221 patients (84.2% female, mean age of 45.4 ±13.5 years, mean disease duration of 15.4±9.5 years). In this preliminary study, the proposed cut-off values of SLE-DAS to define each disease activity category were: remission $\text{SLE-DAS} \leq 2.08$, LDA $2.08 < \text{SLE-DAS} \leq 3.77$, mild disease activity $3.77 < \text{SLE-DAS} \leq 7.64$, and moderate/severe disease activity $\text{SLE-DAS} > 7.64$ (Table 1). The overall accuracy of these SLE-DAS cut-off values to identify each disease activity state was 96.4%. The agreement between SLE-DAS and physician's classification was very high ($k=0.925$, $p<0.001$). Distribution of SLE-DAS and SLEDAI-2K scores in each disease activity state is presented in Figure 1.

According to the SLE-DAS cut-offs, 68.8% of the patients were in remission, 2.3% in LDA, 10.9% in mild disease activity and 18.1% in moderate/severe disease activity.

Abstract THU0267 – Table 1. Performance of SLE-DAS to assess each disease activity state.

Disease activity state	Sensitivity (%)	Specificity (%)	Precision (%)
Remission ($\text{SLE-DAS} \leq 2.08$)	99.3	97.1	98.7
Low Disease Activity ($2.08 < \text{SLE-DAS} \leq 3.77$)	66.7	99.5	80
Mild Disease Activity ($3.77 < \text{SLE-DAS} \leq 7.64$)	88.0	99.0	91.7
Moderate/Severe Disease Activity ($\text{SLE-DAS} > 7.64$)	94.9	98.4	92.5

Conclusion: The SLE-DAS has a high precision in identifying remission, LDA, and other disease activity states in SLE. These results suggest that the SLE-DAS is an accurate tool in defining achievable targets in SLE management.

Figure 1. SLE-DAS and SLEDAI-2K boxplots for each disease activity state according to the physician's classification. The superiority of SLE-DAS to separate the disease activity levels is indicated by the clear separation of its boxplots, in contrast to the overlap of the SLEDAI-2K boxplots.

Abstract THU0267 – Figure 1

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THU0266

CLINICAL AND LABORATORY FEATURES OF PRIMARY SJÖGREN'S SYNDROME ASSOCIATED WITH ANTICENTROMERE ANTIBODIES

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Background: The prevalence of ACA among patients with pSS varies from 2% to 27%. Among experts, there is a lot of controversy about whether primary Sjögren's syndrome with ACA is a separate disease subtype or overlap-syndrome with systemic sclerosis.

Objectives: To evaluate clinical and laboratory features of anticentromere antibody-positive (ACA) primary Sjögren's syndrome (pSS); to evaluate the spectrum of autoantibodies in patients of this group; to evaluate conformity of the patients to the pSS and systemic sclerosis (SSc) classification criteria; to evaluate prevalence of salivary MALT-lymphoma in this group of patients; to evaluate prevalence of primary biliary cirrhosis (PBC)/biliary lesions in this group of patients.

Methods: From 2012 to 2018, we examined 83 patients with pSS and ACA. Inclusion criteria were conformity to the 2001 Russian Sjögren's syndrome criteria and high ACA titer. We used ACR 2012 and ACR/EULAR 2016 criteria to evaluate conformity to the pSS, and ACR 2013 criteria to evaluate conformity to the SSc. Diagnosis of salivary MALT lymphoma was established on the basis of histological, immunohistochemical and PCR studies of biopsy specimens of parotid salivary glands. Diagnosis of PBC/biliary lesions was made on the basis of histological and immunohistochemical studies of liver biopsy specimens.

Results: We found a low detection rate of anti-Ro antibodies (32.5%), anti-La antibodies (7.2%), RF (21.7%), increased ESR (14%), leukopenia (7%), hypergammaglobulinemia (17.6%), increased IgG (9.5%), increased IgA (18.7%) hypocomplementemia (16.1%) in the group of patients with pSS and ACA. Despite the low frequency of detection of the RF, some patients of this group had MALT-lymphoma: 14 patients had salivary MALT-lymphoma (16.8%), one patient had tonsil MALT-lymphoma with nodal involvement (1.2%). In addition, patients of this group are characterized by a high frequency of detection of AMA antibodies 17/52 (32.7%), increased IgM (29.7%) and increased risk of biliary lesions (14.4%). According to our data increased risk of developing biliary lesions (28.5%), primary biliary cirrhosis (28.5%), autoimmune hepatitis (AIH) (28.5%), overlap-syndrome between PBC and AIH (14.5%) was observed in patients with functional signs of liver damage (ALT/AST, GGT, ALP >2N), AMA-positivity, high levels of IgM. Only two patients, who were diagnosed with liver disease according to studies of biopsy specimens, lacked AMA-antibodies. Damage to the nervous system, kidneys, antiphospholipid syndrome, rheumatoid arthritis, hypergammaglobulinemic purpura and cryoglobulinemic vasculitis were much less common and were single. Also patients with pSS and ACA often have Raynaud's phenomenon (54.9%) with capillaroscopic changes of the scleroderma type (68%) and an increased risk of developing limited form of systemic scleroderma (24%).

Conclusion: pSS associated with ACA is a subtype of the disease, significantly different from the "classic" in a number of clinical and laboratory signs and characterized by an increased risk of SSc and PBC/biliary lesions which in some cases leads to the underdiagnosis of pSS. ACA should be considered as pathogenetically related to pSS antibodies and all ACA-positive patients should be examined for pSS and PBC/biliary lesions regardless of whether they have SSc or not. Patients with a significant enlargement of salivary glands should be biopsied to confirm the presence of MALT-lymphoma before initiating hormonal, antilymphoproliferative and anti-B-cell therapy.

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THU0269

SERUM IL-6 AND CIRCULATING IMMUNE COMPLEXES AS BIOMARKERS OF DISEASE ACTIVITY IN MULTI-ETHNIC ASIAN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: IL-6 plays an important role in B cell hyperactivity and immunopathology of systemic lupus erythematosus (SLE), and may have a direct role in mediating tissue damage [1]. Elevated levels of serum

circulating immune complexes (CICs) have been described in SLE but the relationship with disease activity in our multi-ethnic Asian patients remains unclear.

Objectives: To determine the correlation between disease activity and the levels of CICs, serum and urine IL-6 in a Singapore cohort of multi-ethnic Asian SLE patients.

Methods: Serum levels of CICs, IL-6 and urine IL-6 were measured in 88 SLE patients using CIC-C1q and high sensitivity IL-6 ELISAs. All patients fulfilled the 1997 revised American College of Rheumatology (ACR) classification criteria. Clinical and laboratory manifestations, therapy, disease activity and damage at the time of sample collection was collected. Disease activity was scored with the SLE Activity Measure-revised (SLAM-R) and damage with the ACR/Systemic Lupus International Collaborating Clinic SLE damage index (SDI). The correlation between disease activity score and CICs, serum and urine IL-6 were assessed using Spearman's correlation. Receiver operator characteristic (ROC) curve analysis was performed to assess the performance of the individual biomarkers in discriminating SLE disease activity.

Results: The cohort of 88 patients were predominantly female ($n = 78$, 89.6%), with a mean age of $40 \text{ years} \pm 13.1$. The majority were of Chinese ethnicity ($n = 73$, 83%), 13% were Malay ($n = 11$) and 4 individuals were of other races. The mean disease duration was $98.4 \text{ months} \pm 86.4$. The mean scores of SLAM-R and SDI were 2.9 ± 2.2 and 0.9 ± 0.9 respectively. SLE disease manifestations at the time of sample collection included mucocutaneous involvement (5.7%) and active urine sediment (28.7%). 77% had hypocomplementaemia and 70.1% had elevated titres of anti-dsDNA antibody. The majority were on corticosteroids (75.9%) and hydroxychloroquine (65.5%). Immunosuppressive drugs included azathioprine in 37.9%, mycophenolate in 6.9%, intravenous pulse cyclophosphamide in 6.9% and cyclosporin in 1 patient. There was significant positive correlation between SLAM-R and serum CICs ($R = 0.4121$, $p < 0.01$), serum IL-6 ($R = 0.4227$, $p < 0.01$) and urine IL-6 ($R = 0.3142$, $p = 0.01$). Based on the area under the curve (AUC), CICs and urine IL-6 were better in discriminating active SLE (AUC 0.8002, $p < 0.01$ and AUC 0.7397, $p < 0.01$ respectively) compared to serum IL-6 (AUC 0.5554, $p = 0.1718$).

Conclusion: Our study observed significant correlation between levels of serum circulating immune complexes, serum and urine IL-6 with SLE disease activity in our multi-ethnic Asian patient cohort. ROC curve analysis suggests that serum CICs and urine IL-6 may serve as sensitive biomarkers to identify SLE patients at risk of flares.

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THU0270 THE BURDEN OF CHRONIC KIDNEY DISEASE IN SYSTEMIC LUPUS ERYTHEMATOSUS: A NATIONWIDE EPIDEMIOLOGIC STUDY

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Background: Clinical-epidemiological research has advanced our knowledge on the negative impact of lupus nephritis (LN) on systemic lupus erythematosus (SLE) outcomes. Impaired renal function at LN diagnosis and failure to normalize renal function upon aggressive immunosuppressive therapy are associated with a very poor long-term renal outcome. Most reports on that field are however based on tertiary care data of limited sample size that impede the ability to generalize the findings. In order to measure the impact of renal function impairment on clinical outcome such as death or cardiovascular events effectively, updated comprehensive information at national level is needed.

Objectives: We conducted an analysis of a French nationwide database to assess the characteristics associated with the presence of CKD (i.e. eGFR $< 60 \text{ mL/min/1.73m}^2$) and the prognosis associated with CKD in SLE patients.

Methods: Characteristics of all admitted SLE patients experiencing CKD in France from 2009 to 2015 were analyzed through the French medico-administrative database. Factors associated with CKD and major clinical outcomes such as end-stage renal disease (ESRD), cardiovascular event (CVE), septic shock and death were assessed. We used a multivariate Cox proportional

hazard model and subdistribution hazard models to analyze survival without major clinical events according to the presence of CKD.

Results: From 2009 to 2015, 26 320 SLE patients were hospitalized in France. Among them, 6 439 (86.5% women; mean age 45.7 [16.5] years old) had a baseline stay in 2009 during which CKD was reported in 428 (6.7%) cases. Multivariate analysis showed that lupus nephritis (OR 6.6 [5.2-8.4]), high blood pressure (OR 3.5 [2.8-4.5]), septic shock (OR 3.2 [1.7-6.0]) and past cardiovascular history (OR 1.4 [1.0-2.0]) were associated with CKD status.

From 2009 to 2015, ESRD, CVE, septic shock, and death occurred in 4.0%, 14.4%, 6.3% and 9.6% of the 6 439 SLE patients. CKD at baseline was independently and strongly associated with the occurrence of ESRD (sdHR 15.9 [11.6-21.9]), CVE (sdHR 1.7 [1.4-2.2]), septic shock (sdHR 2.1 [1.5-2.8]) and death (HR 1.7 [1.3-2.2]) during the follow up.

Conclusion: CKD is a major risk factor for overall morbidity and mortality in SLE patients, highlighting the need for early pre-CKD lupus nephritis diagnosis and treatment.

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THU0271 SERUM LEVELS OF TRANSFORMING GROWTH FACTOR B (TGF-β) IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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Background: Primary Sjogren's syndrome (pSS) is an autoimmune disease affecting primarily exocrine, especially salivary, glands. The epithelial damage, autoantigens release, activation of innate and acquired immunity form the underlying of the pSS pathogenesis. The main role in pSS is played by B-lymphocytes and production of autoantibodies. One of the cytokines which may play a role in autoimmune processes is tumor growth factor beta (TGF-β), pleiotropic cytokine, which is involved in the control of autoimmune reactions, cell proliferation and the organ accumulation of lymphocytes. Numerous studies focused on the expression of TGF-β in salivary glands, as an organ targeted in pSS.

Objectives: The aim of this study was to evaluate the activity of TGF-β in serum of patients with pSS and to show its significant relationships with other cytokines active in the pathogenesis of this syndrome.

Methods: 33 patients with pSS (according to current EULAR/ACR criteria) were included into the study, female 28 (85%), men 5 (15%), mean age 47 ± 16 . Routine laboratory tests (blood morphology, ESR, CRP, rheumatoid factor) were performed along with ophthalmological assessment (Schirmer's test, ocular staining score) with confirmation of dry eye. Patients had routine chest X-ray and, in case of clinical indications, high resolution computed tomography to assess interstitial changes. Serum concentrations of TGF-β were determined using an Quantikine ELISA Kit. Serum cytokines levels of BAFF, APRIL, FLT-3L, LT-α, IL-21, TNF-α were evaluated using standard ELISA assays. Level of antinuclear antibodies (IF;HEP-2000) was measured; presence of anti-SS-A and anti-SS-B antibodies was determined by semi-quantitative immunoblotting evaluation. Biopsy of minor salivary gland with the histopathological evaluation (focus score-FS) and the immunochemistry (CD3 +, CD4 +, CD19 +, CD21 +, CD35 + cells) was performed. Statistics: differences between groups were analyzed using U Mann-Whitney test (continuous variables). Correlations between quantitative variables were assessed with the Spearman correlation coefficient. Statistical significance $p < 0.05$. The study was approved by the ethics committee.

Results: The negative correlation ($\rho = -0.472$) between TGF-β and TNF-α was demonstrated. There was no correlation between TGF-β and other tested cytokines or autoantibodies (ANA, anti-SS-A, anti-SS-B). There was no correlation between TGF-β and results of ocular examinations, FS and immunochemistry. There was no correlation between TGF-β and lung involvement, especially fibrosis, in this group.

Conclusion: i) results may indicate that TGF-β, influences the serum TNF-α activity in pSS patients, ii) our findings suggest, that TGF-β may