of SLE patients were reported to suffer from severe infections^{1,2}. However, due to the high cost of recruiting patients, we still do not have a holistic picture of the SLE-infection association. Administrative data which encompass all provincially funded healthcare service data shows promising opportunities to advance the knowledge and management of the SLE patients which cannot be evaluated by the conventional clinical setting with small sample size and selective samples^{3,4,5}.

Objectives: To evaluate the risk of severe infection and infection-related mortality among patients with newly diagnosed systemic lupus erythematosus.

Methods: We conducted an age- and gender- matched cohort study of all patients with incident SLE between January 1, 1997 and March 31, 2015 using administrative health data from British Columbia, Canada. Primary outcome was the first severe infection after SLE onset necessitating hospitalization or occurring during hospitalization. Secondary outcomes were total number of severe infections and infection-related mortality.

Results: We identified 5,169 SLE patients and matched them with 25,845 non-SLE individuals from the general population, yielding 955 and 1,986 first severe infections during 48,367 and 260,712 person-years follow-up, respectively. The crude incidence rate ratios for first severe infection and infection-related mortality were 2.59 (95% CI, 2.39-2.80) and 2.20 (95% CI, 1.76-2.73), respectively. The corresponding adjusted hazard ratios were 1.82 (95% CI 1.66-1.99) and 1.61 (95% CI, 1.24-2.08). SLE patients had an increased risk of a greater total number of severe infections with crude rate ratio of 3.24 (95% CI, 3.06-3.43) and adjusted rate ratio of 2.07 (95% CI, 1.82-2.36).

Conclusion: SLE is associated with increased risks of first severe infection (1.8-fold), a greater total number of severe infections (2.1-fold) and infection-related mortality (1.6-fold).

REFERENCES:

- [1] Yurkovich M, Vostretsova K, Chen W, Aviña-Zubieta JA. Overall and cause-specific mortality in patients with systemic lupus erythematosus: a meta-analysis of observational studies. *Arthritis Care Res (Hoboken)* 2014;66(4):608-16.
- [2] Petri M. Infection in systemic lupus erythematosus. *Rheum Dis Clin North Am* 1998;24(2):423-56.
- [3] Cervera R, Khamashta MA, Font J, et al. Morbidity and mortality in systemic lupus erythematosus during a 10-year period: a comparison of early and late manifestations in a cohort of 1,000 patients. *Medicine (Baltimore)* 2003;82(5):299-308.
- [4] Goldblatt F, Chambers S, Rahman A, Isenberg DA. Serious infections in British patients with systemic lupus erythematosus: hospitalisations and mortality. *Lupus* 2009;18(8):682-9.
- [5] Bosch X, Guilabert A, Pallares L, et al. Infections in systemic lupus erythematosus: a prospective and controlled study of 110 patients. *Lupus* 2006;15(9):584-9.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.17

OP0044

ANA POSITIVITY IS ASSOCIATED WITH COMPLEX IMMUNE DISTURBANCE EVEN IN INDIVIDUALS WHO DO NOT DEVELOP CLINICAL AUTOIMMUNE DISEASE

S. U. Hassan^{1,2}, Z. Wigston¹, A. Burska¹, M. Y. MD Yusof^{1,2}, E. Vital^{1,2}. ¹Leeds Institute of Rheumatic and Musculoskeletal Medicine, Rheumatology, Leeds, United Kingdom; ²NIHR Leeds Musculoskeletal Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom

Background: Study of pre-clinical autoimmunity can reveal immune changes that initiate or prevent clinical disease. We previously reported an At Risk cohort of ANA positive individuals referred to secondary care, of whom 16% progressed to SLE or Sjogren's syndrome during follow up[1]. Recently, we also reported that even ANA positive individuals who do not develop clinical autoimmunity, have defective pDC function and non-haematopoietic interferon-production[2].

Objectives: To describe the immunophenotype of ANA-positive progressors and non-progressors compared to healthy controls.

Methods: We conducted a prospective observational longitudinal study of At-Risk individuals in Leeds (n=150) over 3 years with annual follow up. Those who met classification criteria for autoimmune connective tissue disease (AI-CTD) during follow up were termed progressors and others; non-progressors. Among the non-progressors, those with no clinical diagnostic criteria at any time point were called absolute non-progressors (ANP).

At baseline we analysed two IFN-stimulated gene expression scores previously described[3] and flow cytometry performed for major circulating subsets. Association between progression group and biomarkers were tested using independent samples t-test.

Results: 3 year follow up data were available in 148/150 patients. Outcomes were: progressors: 30/148 (20%) [SLE=25; pSS=5] and non-progressors: 118/148 (80%). Within the non-progressors, 69/148 (47%) were ANP.

A detailed analysis of baseline biomarkers is included in Table 1. Despite not developing clinically significant disease, non-progressors had significant alterations in several biomarkers. This was also evident in the ANP sub-group.

Table 1.

Biomarker	Healthy Controls	Non-progressors	Difference from healthy controls	Absolute non-progressors	Difference from healthy controls	Progressors	Difference from healthy controls
	Mean (95% CI)	Mean (95% CI)	p	Mean (95% CI)	p	Mean (95% CI)	p
IFN score A	-6.27 (-6.88, -5.65)	-5.22 (-5.64, -4.80)	0.016	-5.11 (-5.91, -4.32)	0.120	-4.14 (-5.11, -3.18)	0.001
IFN score B	-5.43 (-6.00, -4.85)	-5.30 (-5.62, -4.98)	0.193	-4.96 (-5.45, -4.47)	0.949	-4.27 (-4.90, -3.65)	0.136
% Mono-cytes	14.80 (10.50, 19.11)	15.46 (12.96, 17.97)	0.187	14.94 (11.42, 18.47)	0.738	10.36 (7.42, 13.30)	0.227
% CD4	62.90 (57.75, 68.05)	64.89 (60.86, 68.92)	0.001	68.72 (62.97, 74.47)	0.267	60.93 (53.64, 68.21)	0.001
T cells	32.18 (27.47, 36.90)	28.60 (25.12, 32.09)	0.135	25.02 (20.28, 29.77)	0.044	31.51 (25.63, 37.40)	0.875
% Naive	65.59 (56.56, 74.61)	73.74 (70.02, 77.46)	0.001	76.86 (72.21, 81.51)	0.128	68.86 (60.62, 75.84)	0.173
% Memory	29.56 (20.42, 38.72)	19.72 (15.84, 23.61)	<0.000	23.13 (16.65, 29.61)	0.054	25.57 (17.18, 33.96)	0.163
% B cells	1.12 (0.81, 1.43)	0.91 (0.58, 1.24)	0.964	1.01 (0.44, 1.58)	0.457	0.81 (0.53, 1.10)	0.112
% NK cells	13.65 (9.65, 17.65)	12.30 (8.90, 15.71)	0.480	12.35 (6.65, 18.05)	0.781	11.90 (8.65, 15.14)	0.195

Conclusion: Clinically benign ANA positivity is a complex immune state with many features seen in active SLE, including pDC exhaustion, keratinocyte interferon production and strong skin interferon score, increased blood interferon score, and disturbance of B cell subsets. These findings suggest that other factors are necessary for clinical disease, or that regulatory mechanisms stabilise autoimmunity. Further work in this cohort will address these questions.

REFERENCES:

- [1] Md Yusof et al. *Ann Rheum Dis* 2018
- [2] El-Sherbiny et al. *Sci Rep* 2018
- [3] Psarras et al. *Nat Commun*. 2020

Disclosure of Interests: Sabih-UI Hassan: None declared, Zoe Wigston: None declared, Agata Burska: None declared, Md Yuzaiful Md Yusof: None declared, Edward Vital Grant/research support from: Honoraria and research grant support from Roche, GSK and AstraZeneca.

DOI: 10.1136/annrheumdis-2021-eular.1414

OP0045

NLRP12 INVOLVES IN THE LUPUS WITH POSITIVE INTERFERON SIGNATURE

Y. P. Tsao¹, F. Y. Tseng², C. W. Chao², M. H. Chen¹, S. T. Chen². ¹Taipei Veterans General Hospital, Division of Allergy, Immunology and Rheumatology, Department of Medicine, Taipei, Taiwan, Republic of China; ²National Yang-Ming University, Institutes of Clinical Medicine, Taipei, Taiwan, Republic of China

Background: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease with diverse etiological factors. It was recognized that interferon (IFN) signature involved in the progress of SLE. NLRP12 (NOD-like receptor family (NLR) pyrin domain containing 12) is a pyrin containing NLR protein that we had linked its new biological function to the cross-regulation of Toll like receptor (TLRs) and Rig-I like receptor (RIG-I) pathways. NLRP12 acts as an innate immune check-point in regulating type I IFNs expression during TLRs and RIG-I activation. The importance of NLRP12 in lupus disease activity remained to be elucidated.

Objectives: To clarify the role of NLRP12 in regulating the interferon signature.

Methods: Peripheral blood mononuclear cells (PBMCs) were collected from SLE patients and healthy donors for analysis of NLRP12 and IFN- α gene expression by RT-QPCR. PBMCs were applied for Chromatin immunoprecipitation (ChIP) assay and electrical mobility shift assay (EMSA) to determine the putative transcription factor that regulates NLRP12 expression. An involvement of epigenetic regulation of NLRP12 expression in SLE patients was also analyzed. Bone marrow derived dendritic cells (BMDCs) were collected from wild type mouse and Nlrp12 knocked-out mice. Another CD14+ monocytes were isolated from 10 cases of lupus patients and 8 cases of healthy control, following by stimulating different type of nucleic acids, and IFN- α and IL-6 were measured with ELISA assay. CD14+ monocytes in lupus patients were also pre-treated with IFNAR2 antibody for further nucleic acid stimulation. Two mice models were applied for evaluation the role of Nlrp12: intraperitoneal injection of TMPD (2,6,10,14-tetramethylpentadecane, or pristane) in C57BL/6 mice and Fas^{lpr} mice. Both models were conducted with and without Nlrp12 knockout.

Results: *NLRP12* expression was significantly lower in PBMC isolated from SLE patients compared to healthy donors. The inverse correlation was observed in *NLRP12* and *IFNA* gene expression as well as *NLRP12* expression and amount of double-stranded DNA autoantibody in SLE patients. *NLRP12* expression showed negative correlations with IFN- α treatment, as well as herpes simplex virus-1 (HSV-1) infection. Results from ChIP and EMSA analysis indicated a potential transcription factor 1 (TF-1) regulating *NLRP12* promoter activity. TF-1 lead to transcriptional suppression of *NLRP12* in SLE PBMC, and it was gradually induced after IFN treatment. Recruitment of TF-1 to *NLRP12* promoter in SLE PBMC compared to the healthy PBMC was detected, and increased when treating with IFN. Human CD14⁺ monocytes collected from lupus and healthy control stimulating with different type of nucleic acids revealing significant increasing level of IFN- α and IL-6 in lupus patients. Among animal models, both pristine induced mice and Fas^{lpr} mice revealed increasing autoantibodies production and severity of glomerulonephritis in *Nlrp12*^{-/-} group in comparison with *Nlrp12*^{+/+} ones, indicating the role of *NLRP12* in maintaining positive interferon signature as well as disease activity.

Conclusion: Expression level of *NLRP12* has been demonstrated to be a biomarker of disease activity in SLE patients. The *NLRP12* was involved in the interferon signature, which was also negatively regulated by TF-1. Both clinical samples and animal models revealed *NLRP12* in maintaining the positive interferon signature, indicating the possible role of exacerbating factor for lupus disease activity.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4215

Clinical aspects of axial spondyloarthritis – science meets daily practice

OP0046

CAN PATIENTS WITH AXIAL SPONDYLOARTHRITIS INDICATE WHETHER PAIN IS MAINLY RELATED TO INFLAMMATION OR STRUCTURAL DAMAGE?

A. Kampman¹, F. Wink^{1,2}, M. Carbo², F. Maas², A. Spoorenberg², S. Arends².

¹Medical Center Leeuwarden, Rheumatology, Leeuwarden, Netherlands;

²University Medical Center Groningen, Rheumatology and Clinical Immunology, Groningen, Netherlands

Background: Patients with axial spondylarthritis (axSpA) mainly rate disease activity on experienced symptoms such as pain (1). Pain is also included in the assessments (ASDAS and BASDAI) used to monitor disease activity in axSpA. However, besides disease activity, also other factors including the presence of structural damage may be related to experienced pain and discomfort.

Objectives: To explore to what extent axSpA patients relate their experienced pain in neck, back and hips to inflammation and/or structural damage.

Methods: Patients from the Groningen Leeuwarden Axial Spondyloarthritis (GLAS) cohort visiting the out-patient clinic between May 2016 and October 2019 were included in this cross-sectional analysis. Patients filled out two additional questions related to question 2 of the BASDAI: To what extent do you think pain in your neck, back and hips is related to: 1. inflammation caused by axSpA?, 2. damage of spine and joints caused by axSpA? These questions were answered on a NRS from 0 (none) to 10 (very much). A difference of ≥ 2 points was considered as clinically relevant. Patients who differentiated the cause of their pain were allocated to an inflammation or damage group, in favour of their highest score. Furthermore, patient characteristics and clinical assessments were compared between the inflammation and damage groups.

Results: In total, 688 axSpA patients were included, 62.4% were male, mean age was 47.9 years, median symptom duration was 19 years, 77.9% were HLA-B27+, mean BASDAI was 3.9 and mean ASDAS_{CRP} was 2.3. Respectively 13% and 14% of the patients reported a score of 0 on the additional questions about inflammation or damage.

In total, 517 (75%) patients could not differentiate between inflammation or damage. 102 (15%) patients interpreted experienced pain as mainly related to inflammation and 69 (10%) patients interpreted their pain as mainly related to structural damage.

Patients who interpreted pain as mainly related to inflammation were significantly younger, had shorter symptom duration, were more frequently diagnosed as non-radiographic axSpA and had higher ASDAS_{CRP}, which was driven by the patient-reported questions as the objective marker CRP was not significantly different between both groups (Table 1).

Table 1. Patients characteristics and clinical assessments of axSpA patients who related pain mainly to inflammation versus to structural damage.

	Inflammation group (n = 102)	Structural damage group (n = 69)	P-value
Age (years)	39.5 $\pm$ 12.4	48.9 $\pm$ 12.4	<0.001
Symptom duration (years)	12 (6 – 20)	28 (17 – 35)	<0.001
Diagnosis non-radiographic axSpA	39 (40%)	8 (13%)	<0.001
Male gender	60 (59%)	44 (64%)	0.627
BASDAI	4.2 $\pm$ 1.8	3.9 $\pm$ 2.0	0.371
BASDAI – Q2	6 (3 – 7)	4 (2 – 6)	0.005
Patient global disease activity	4 (3 – 7)	3 (2 – 5)	<0.001
ASDAS _{CRP}	2.6 $\pm$ 0.9	2.2 $\pm$ 0.8	0.003
CRP	3.0 (2.0 – 8.0)	2.5 (2.0 – 4.4)	0.094
Occiput wall distance (cm)	0.0 (0.0 – 4.0)	4.0 (0.0 – 10.0)	<0.001
Chest expansion (cm)	5.8 (4.0 – 7.0)	4.0 (3.0 – 6.0)	0.006
Modified Schober test (cm)	14.0 $\pm$ 1.6	13.5 $\pm$ 1.6	0.052
Lateral flexion mean (cm)	15.3 $\pm$ 6.5	12 $\pm$ 5.9	0.001
Cervical rotation mean (degrees)	80 (70 – 90)	70 (45 – 81)	<0.001
mSASSS *	3.0 (0.0 – 9.0)	8.0 (1.8 – 26.0)	0.061

* only available in a subgroup of patients. Inflammation group (n=31), structural damage group (n=39).

Patients who reported their pain as mainly related to structural damage showed significantly worse spinal mobility on almost all spinal mobility tests. In the subgroup of patients with available mSASSS data, there was also a trend towards more spinal radiographic damage (Table 1).

Conclusion: In our large observational cohort of axSpA patients, the vast majority (75%) could not rate whether experienced pain in neck, back and hips was more related to inflammation or structural damage. However, if patients were able to relate pain to inflammation or damage, it seems in accordance with the outcome of their clinical assessments.

REFERENCES:

[1] Spoorenberg A *et al.* Rheumatology (Oxford), 2005;44(6):789-95.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.293

OP0047

IDENTIFICATION OF CLINICAL PHENOTYPES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS, PERIPHERAL SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS ACCORDING TO PERIPHERAL MUSCULOSKELETAL MANIFESTATIONS: A CLUSTER ANALYSIS IN THE INTERNATIONAL ASAS-PERSPA STUDY

C. López-Medina¹, S. Chevre², A. Moltó¹, J. Sieper³, M. T. Duruöz⁴, U. Kiltz⁵, B. Zorkany⁶, N. Hajjaj-Hassouni⁷, R. Burgos-Vargas⁸, J. Maldonado-Cocco⁹, N. Ziade¹⁰, M. Gavalí¹¹, V. Navarro-Compán¹², S. F. Luo¹³, A. Biglia¹⁴, T. J. Kim¹⁵, M. Kishimoto¹⁶, F. Pimentel Dos Santos¹⁷, J. Gu¹⁸, L. Muntean¹⁹, F. A. Van Gaalen²⁰, P. Géher²¹, M. Magrey²², S. Ibáñez²³, W. Bautista-Molano²⁴, W. P. Maksymowych²⁵, P. M. Machado²⁶, R. B. M. Landewé²⁷, D. Van der Heijde²⁰, M. Dougados¹. ¹Cochin Hospital, Rheumatology, Paris, France; ²University of Paris, INSERM (U1153): Clinical Epidemiology and Biostatistics, Paris, France; ³Charité University, Department of Gastroenterology, Infectious Diseases and Rheumatology, Berlin, Germany; ⁴Marmara University School of Medicine, PMR Department, Rheumatology Division, Istanbul, Turkey; ⁵Rheumazentrum Ruhrgebiet, Ruhr-University Bochum, Rheumatology, Herne, Germany; ⁶Cairo University, Cairo, Egypt; ⁷Health Sciences College, International University of Rabat (UIR), Rabat, Morocco; ⁸Hospital General de México Eduardo Liceaga, Rheumatology, Mexico City, Mexico; ⁹Buenos Aires School of Medicine, Rheumatology, Buenos Aires, Argentina; ¹⁰Rheumatology, Saint-Joseph University and Mount Lebanon Hospital, Beirut, Lebanon; ¹¹Nizam's Institute of Medical Sciences, Rheumatology, Hyderabad, India; ¹²Rheumatology, University Hospital La Paz, Madrid, Spain; ¹³Chang Gung Memorial Hospital-Linkou, Rheumatology, Allergy and Immunology, Taoyuan, Taiwan, Republic of China; ¹⁴Fondazione IRCCS Policlinico S. Matteo, University of Pavia, Rheumatology, Pavia, Italy; ¹⁵Chonnam National University Medical School and Hospital, Rheumatology, Donggu Gwangju, Korea, Rep. of (South Korea); ¹⁶Kyoin University School of Medicine, Department of Nephrology and Rheumatology, Tokyo, Japan; ¹⁷Nova University of Lisbon, NOVA Medical School, Lisboa, Portugal; ¹⁸Third Affiliated Hospital of Sun Yat-Sen University, Rheumatology, Guangzhou, China; ¹⁹Iuliu Hatieganu University of Medicine and Pharmacy, Rheumatology, Cluj-Napoca, Romania; ²⁰Leiden University Medical Center, Rheumatology, Leiden, Netherlands; ²¹Semmelweis University, Rheumatology, Budapest, Hungary; ²²Cases Western Reserve University School of Medicine, Rheumatology, Cleveland, United