POS0758

DOES EXPERIENCE IN SYSTEMIC LUPUS ERYTHEMATOSUS INFLUENCE THE PHYSICIAN GLOBAL ASSESSMENT SCORING? A CROSS-SECTIONAL STUDY ON TWO EUROPEAN COHORTS

E. Chessa¹, M. Piga¹, F. Sagez², R. Felten², A. Floris¹, A. Cauli¹, L. Arnaud². ¹Rheumatology Unit, AOU and University of Cagliari, Department of Medical Sciences and Public Health, Cagliari, Italy; ²Hôpitaux Universitaires de Strasbourg, Université de Strasbourg, Service de Rhumatologie, Centre National de Référence des Maladies Systemiques et Autoimmunes Rares Est Sud-Ouest (RESO), Strasbourg, France

Background: The Physician Global Assessment (PGA) is an outcome instrument based on physician judgement of disease activity in patients with Systemic Lupus Erythematosus (SLE). Due to the subjectivity of the score and lack of standardization, the PGA could represent a source of heterogeneity, because the same manifestations could be rated differently by physicians with different backgrounds (1).

Objectives: The purpose of this study was to evaluate the inter-rater reliability of PGA between a rheumatology trainee and rheumatologists expert in SLE from 2 european countries.

Methods: SLE patients classified according to SLICC 2012 criteria were enrolled between May 2019 and December 2019 during a SLEuro traineeship program. Demographic, clinical (SLEDAl-2k, PGA), serological and ongoing medication data were collected. PGA was evaluated before (pre-lab) and after (post-lab) knowledge of laboratory exams, using a Visual Analogue Scale (VAS) ranging from 0 to 3, anchored at point 1 (mild), 2 (moderate) and 3 (severe activity). A trainee in Rheumatology (EC) and three rheumatologists experts in SLE (LA, MP, FS) independently scored the PGA for each patient.

The trainee preliminarily received a standardization training with her tutor (MP), consisting of a shared discussion about 10 consecutive SLE outpatients to increase reliability in PGA scoring.

Inter-rater reliability was analysed using the intraclass correlation coefficient (ICC) with a two-way single-rating model (2,1); 95% confidence interval (CI) was calculated.

Results: Fifty-seven patients (86% female) affected from SLE (29 belonging to a French cohort and 28 to an Italian cohort) with a mean (SD) age 43.2 (15.9) years and a median [IQR] disease duration 6.4 [2.0-15.4] years were enrolled. Clinical features are presented in table 1. Pre-lab PGA scores were obtained from all patients and ranged from 0 to 2.3; post-lab PGA scores were obtained from 51 patients and ranged from 0 to 2.9. Inter-rater reliability of the PGA among the trainee was good to excellent for each lupus expert comparison: a) pre-lab PGA ICC 0.94, 95% CI 0.87-0.97; post-lab PGA ICC 0.94, 95% CI 0.87-0.97 (MP); b) pre-lab PGA ICC 0.84, 95% CI 0.63-0.93; post-lab PGA ICC 0.96 CI 0.88-0.99 (LA); c) pre-lab PGA ICC 0.91, 95% CI 0.65-0.98; post-lab PGA ICC 0.91, 95% CI 0.65-0.98 (FS).

Conclusion: After an adequate standardization, PGA scoring reaches good to excellent reliability between trainee and experts.

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Clinical Data

Caucasian	44 (77.2%)
anti-dsDNA titre (median,IQR)	14 (0-75)
Hypocomplementemia (n,%)	30 (54%)
SLEDAl≥6 (n,%)	18 (31.6%)
SLEDAl (median,IQR)	4 (2-6)
Flares (n,%)	18 (31.6%)
Ongoing prednisone treatment (n,%)	41 (71.9%)
Prednisone dose mg (mean±sd)	5 (0 - 8.9)
Hydroxychloroquine (n,%)	44 (77.2%)
Immunosuppressant (n,%)	35 (61.4%)

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POS0759

THE JOURNEY OF PATIENTS FROM FIRST SYMPTOMS TO DIAGNOSIS OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): AN OBSERVATIONAL STUDY

N. Kapsala¹, S. Flouda¹, D. Nikolopoulos¹, K. Chavatzas¹, A. Pieta¹, A. Grivas¹, A. Ntourou¹, K. Togia¹, P. Rapsomaniki¹, T. Gerogianni¹, D. Tseronis¹, M. Aggelakos¹, T. Karageorgas¹, P. Katsimpri¹, G. Bertisias², A. Fanouriakis^{1,3}, D. Boumpas¹. ¹"Attikon" University Hospital of Athens, Rheumatology and Clinical Immunology, Medical School, National and Kapodistrian University of Athens, Athens, Greece; ²University of Crete, Rheumatology, Clinical Immunology and Allergy, Heraklion, Greece; ³"Asklepieion" General Hospital, Department of Rheumatology, Voula, Athens, Greece

Background: The lack of pathognomonic features poses a considerable challenge in SLE diagnosis. The time from symptom onset to diagnosis has been reported to range from two to six years¹.

Objectives: To document the initial symptoms of the disease and the time lapse until its diagnosis.

Methods: We examined 438 patients from the "Attikon" SLE cohort². For diagnosis, we used the classification criteria (ACR, SLICC, EULAR-ACR) or in few cases clinical diagnosis (n=32, 7.3%). Data were collected using patient interviews, in-person clinical visits and medical charts review. Initial symptoms were recorded and determined chronologically using prespecified forms with a list of typical manifestations (skin, joints, renal, nervous system, pleuropulmonary, cardiovascular, anti-phospholipid syndrome) as well as characteristic disease features (Raynaud's phenomenon, fatigue, fever, sicca symptoms). Questions also included the time between symptom onset and initial physician visit, the time from first medical consultation until first rheumatologist assessment, the time from rheumatologist assessment to SLE definite diagnosis, the number of physicians seen before SLE diagnosis, the specialty of first physician and of diagnosing physician. Information on demographic and clinical characteristics, disease activity and disease damage, was collected both at enrolment and at last follow-up visit.

Results: 88.5% of patients were females, mean (±SD) age at diagnosis was 41.9 years ± 15.4 and disease duration was 6.7 ± 7 years. Most common systems involved were joints (94.5%), skin (73.7%), blood (39.2%) and renal (17.5%). At diagnosis, 9.8% of patients were ANA negative. The most common initial symptoms at disease onset were arthritis/arthralgia (74.4%), followed by fatigue (53.1%) and photosensitive rash (50.9%) (Table 1). Among non-criteria features, Raynaud's phenomenon was reported by 146 patients (33.3%) prior the diagnosis. The median interval between symptoms onset and the SLE diagnosis was 16 months (IQR 5-60). SLE was diagnosed earlier in ANA-positive than -negative patients [median time 14 months (IQR 5-60) vs 36 months (IQR 10.5-84); P=0.1, t-test]. Approximately half of the patients (52.5%) were diagnosed after 12 months from disease onset with only 15.9% diagnosed within 3 months of symptoms presentation. The median lag time between onset of symptoms and the first medical consultation was 2 months (IQR 1-12). Internists were the most common first consultants (27.8%) followed by orthopedists (15.9%), dermatologists (13.6%) and rheumatologists (13.4%). The median interval between the first medical assessment and first rheumatologist evaluation was 3 months (IQR 0-11.5) while the median time from rheumatologist assessment to definite diagnosis was 0 months (IQR 0-4). SLE patients consulted an average of 3 different physicians before the definite diagnosis, which in 95.8% was established by rheumatologists.

Conclusion: Approximately 50% of patients were diagnosed with SLE after 12 months from symptom onset with a mean time from symptoms to definite diagnosis almost 4 years. Increasing awareness of internists to SLE and avoidance of strict adherence to ANA as a requirement for diagnosis may improve early diagnosis.

Table 1. Initial symptoms prior to diagnosis

Symptoms	N=438 (%)	Duration* (mean months $\pm$ SD)
Arthralgias	326 (74.4)	37.5 $\pm$ 69.4
Photosensitive rash	223 (50.9)	30.6 $\pm$ 70.2
Malar rash	168 (38.3)	22.6 $\pm$ 62
Alopecia	167 (38.1)	19.6 $\pm$ 54.6
Ulcers	106 (24.2)	16.8 $\pm$ 54.4
Fever	103 (23.5)	9.3 $\pm$ 43.8
Raynaud's phenomenon	146 (33.3)	22.3 $\pm$ 68.5
Fatigue	233 (53.1)	19.7 $\pm$ 45.7

*Mean time from symptom onset to established diagnosis

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POS0760

MONITORING C3 AND C4 VARIATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS PREGNANCIES IS USEFUL TO RECOGNIZE COMPLICATIONS. DATA FROM 2 ITALIAN CENTERS

F. Crisafulli¹, R. Reggia², M. Filippini¹, M. Fredi¹, M. C. Gerardi¹, R. Gorla¹, M. G. Lazzaroni¹, D. Lini¹, C. Nalli¹, M. Taglietti¹, A. Lojaco³, S. Zatti³, C. Zanardini³, C. Tani⁴, D. Zucchi⁴, M. Mosca⁴, F. Franceschini¹, L. Andreoli¹, A. Tincani¹. ¹ASST Spedali Civili and University of Brescia, Rheumatology and Clinical Immunology Unit, Brescia, Italy; ²Casa di Cura San Camillo, Internal Medicine, Cremona, Italy; ³ASST Spedali Civili and University of Brescia, Obstetrics and Gynecology Unit, Brescia, Italy; ⁴University of Pisa, Rheumatology Unit, Pisa, Italy

Background: In SLE pregnancies adverse pregnancy outcomes (APO) are more frequent than in general obstetric population (GOP). In clinical practice, low C3 and C4 levels are associated with active disease and, during pregnancy, complement activation products are shown to be associated with APO.

Objectives: To analyse complement variations during SLE pregnancies, focusing on disease flares and APO.

Methods: Data on SLE pregnancies prospectively-followed by multidisciplinary team in 2 Italian Centers from 1987 to 2018 were retrospectively analysed. C3 and C4 normal levels were calculated in general obstetric population (GOP) as previously described¹, and related to maternal and fetal outcome. Non categorical variables were compared using Mann-Whitney test or Wilcoxon test when appropriate.

Results: Two hundred forty-six pregnancies in 172 SLE patients were analysed (mean age at conception 31.3 $\pm$ 4.9 years; mean disease duration 8.3 $\pm$ 7.1). Anti-Ro antibodies were positive in 64 patients (37%) and anti-phospholipid antibodies (aPL) were positive in 84 (48%), with single positivity in 54%, double in 24% and triple in 21%; 9 patients (5%) had also a diagnosis of obstetric-antiphospholipid syndrome (APS) and 8 (4%) had thrombotic-APS. Seventy-one patients (41%) had history of Lupus Nephritis.

Thirty-five flares were recorded in 30 pregnancies (12%). APO occurred in 47 pregnancies (19%) and were: 27 fetal loss (20 early miscarriage <10th week and 7 intrauterine fetal death), 11 severe preterm birth (<34th week) and 15 hypertensive disorder (11 pre-eclampsia and 5 pre-eclampsia+HELLP syndrome).

Figure 1. Variations of C3 and C4 median levels (mg/dL) throughout pregnancy in GOP¹ and in SLE pregnancies without and with flare (a) and without and with APO (b).

In GOP, C3 progressively increased throughout pregnancy and C4 increase from the 1st trimester to the 2nd trimester, as well as in SLE pregnancies without flares and without APO, from preconception (Fig 1). In the other SLE groups, C3 and C4 showed a different trend: in pregnancies with flares, they did not increase from preconception to the 1st trimester; in fetal losses and severe pre-term births, they remained stable throughout pregnancy; in hypertensive disorders they increased only between preconception and the 1st trimester.

C3 and C4 levels were higher in GOP than in all SLE pregnancies groups (including those without flares and without APO) in each trimester. SLE pregnancies without flares showed higher C3 and C4 levels than pregnancies with flares, at preconception and in each trimester. SLE pregnancies without APO had higher C3 and C4 levels than pregnancies with fetal death at 2nd trimester, higher C3 levels than severe pre-term births in each trimester and higher C4 at 3rd trimester (Fig.1).

At preconception, pregnancies with flares showed a higher frequency of low C3 and of low C4 than in pregnancies without flares (76% vs 42%, p=0.01; 76% vs 26%, p<0.001, respectively). Using the normality range previously calculated in GOP, SLE pregnancies with flares had higher frequency of low C4 in every trimester as compared with pregnancies without flares (1st: 82% vs 48%, p=0.003; 2nd: 82% vs 64%, p=0.01; 3rd: 64% vs 30%, p=0.002). At multivariate analysis, low C4 at preconception was associated with flare (OR [95% CI]: 10.34 [2.52-42.39]; p=0.001).

* p < 0.05

^ as compared with SLE groups: p<0.05; \$ as compared with SLE pregnancies without flare: p<0.05; + as compared with SLE pregnancies without APO: p<0.05

Conclusion: In SLE pregnancies, monitoring of C3 and C4 is important: its failure to increase can be useful to recognize potential risk situations which deserve particular monitoring.

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