POS0783

LUPUS NEPHRITIS: HISTOLOGICAL FEATURES AND LONG TERM OUTCOMES IN A LARGE SINGLE-CENTRE COHORT

A.I. Cella¹, F.R. Spinelli¹, C. Garufi¹, S. Truglia¹, V.A. Pacucci¹, F. Ceccarelli¹, C. Pirone¹, F. Natalucci¹, M. Speziali¹, C. Alessandri¹, F. Conti¹. ¹Department of Clinical Internal, Anaesthesiological and Cardiovascular Sciences, Sapienza University, Rome, Italy

Background: In Systemic Lupus Erythematosus (SLE) patients the incidence of lupus nephritis (LN) is about 40% ⁽¹⁾. The rate of progression to end stage renal disease (ESRD) is 4.3-10.1% ⁽²⁾ and renal involvement is a strong predictor of morbidity and mortality.

Objectives: To describe clinical, histological features and renal outcomes of LN patients included in our single-center registry reporting data from more than 30 years. Moreover, we examined the correlation between clinical features at LN diagnosis and therapeutic lines used during the course of a 24 years follow-up.

Methods: A total of 71 patients were diagnosed with LN from 1989 to 2020. Demographic features and laboratory abnormalities (serum creatinine, 24 hours urine protein, urinary sediment, ds-DNA) at the time of LN diagnosis and at last available follow-up, were evaluated. We also examined renal biopsy performed and the histological classes (proliferative vs non-proliferative). We considered the increase number of therapeutic lines adopted as a negative prognostic factor in response to therapy. Mean (SD) or median (IQR) were used according the variable distribution. T-test and Chi square and Mann-Whitney were used and p-value <0.05 were considered significant.

Results: Among 71 patients with LN, 63 (88.7%) were females and 8 (11.3%) males, with a F/M ratio of 6. Median SLE duration was 180 (162) months. The median age at the onset of nephritis was 28 (19.5) years and occurred in median after 12 (60) months from SLE diagnosis.

Sixty patients underwent a biopsy: the histology showed class III or IV proliferative glomerulonephritis in 49 patients (81.6%) and a non-proliferative class in 11 (18.3%) (p< 0.0001). Median serum creatinine value, 24 hours urine protein, urinary sediment, anti-ds-DNA at LN onset are reported in Table 1. Induction therapy was performed with cyclophosphamide in 14.5% of cases, mycophenolate in 21.1%, rituximab in 1.3%, cyclosporine A in 1.9% and azathioprine in 4.6%. The lines of therapies adopted during the follow-up ranged between a minimum of 0 and a maximum of 6 lines with a median value of 1.

Overall, the median follow-up was 180 (111) months and 30 (21.3%) patients had at least 120 months of follow-up. Median serum creatinine value, 24 hours urine protein, urinary sediment and eGFR last available follow-up are reported in Table 1. Three patients underwent dialysis and 3 kidney transplantation.

Eight patients underwent a re-biopsy: 7 (87.5%) had a proliferative class and 1 (12.5%) had a membranous class (p=0.01). Median serum creatinine value, 24 hours urine protein, urinary sediment at re-biopsy are reported in Table 1. In re-biopsied subgroup patients, induction therapies were cyclophosphamide in 50% of cases, mycophenolate in 12.5%, cyclosporine A in 25% and azathioprine in 12.5%. There were not statistically significant differences among the age on LN onset, the time from renal onset to the onset of the disease and the number of therapeutic lines adopted (Figure 1).

Conclusion: Among patients with LN the proliferative classes are the most common. At the 15-year follow-up 2,1% had renal transplantation and 2,1% dialysis. We did not detect any association between age at diagnosis, time from renal impairment and the number of therapeutic lines.

REFERENCES:

- [1] Fanouriakis A et al. Update EULAR/ERA-EDTA recommendations for the management of lupus nephritis. Ann Rheum Dis 2019.
- [2] Hanly JG et al. The frequency and outcome of lupus nephritis: results from an international inception cohort study. Rheumatology 2016.

Table 1. Laboratory features in SLE patients at LN onset, at last available follow-up and in re-biopsied patients.

	LN onset (n 71)	AFTER 10 years long FOLLOW-UP (n 30)	Re-biopsied patients (n 8)
Serum creatinine (mg/dl)	0.81 (+/- 0.4)	0.87 (+/- 0.60)	0.07 1.05 (0.45)
24 hours urine protein (mg/24h)	3000 (+/- 3707)	330 (+/- 793)	<0,00001 5068 (2392)
Active urinary sediment	64 patients (45,44%)	2 patients (6.66%)	<0,00001 8 patients (100%)
Anti-ds-DNA + eGFR <50ml/h	30 patients	12 patients (3.6%)	

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3710

POS0784

AUDIOLOGIC EVALUATION IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS AND IMPACT OF HYDROXYCHLOROQUINE THERAPY

S. Tharwat¹, W. Elshawaf², M. K. Nassar³. ¹Mansoura University, Internal Medicine, Rheumatology & Immunology, Mansoura, Egypt; ²Mansoura University, Audiology Unit, ORL Department, Mansoura, Egypt; ³Mansoura

University, Mansoura University Nephrology and Dialysis Unit, Internal Medicine Department, Mansoura, Egypt

Background: Hydroxychloroquine (HCQ) is a commonly used agent in the treatment of rheumatic diseases including systemic lupus erythematosus (SLE). **[1]** **Objectives:** The aim of this study was to evaluate the hearing function in SLE patients and assess the impact of chronic HCQ.

Methods: This study was carried out on 60 individuals (48 SLE and 12 healthy controls). The SLE patients were divided into HCQ group (n=36) and non-HCQ group (n=12) according to the chronic administration of HCQ. All participants were assessed by full audiological history and extended high frequency audiometry at frequencies 9, 10, 11, 2, 12.5, 14, 16, 18 and 20 KHz.

Results: When comparing the study SLE patients with healthy controls, there was a statistically significant difference regarding patient reported otological manifestations such as tinnitus (p=.021), vertigo (p=.002) and hearing impairment (p=.042) while there was no significant difference regarding deafness or ear buzzing in one or both ears. HCQ group showed more hearing impairment at frequency 9000 and 20000 Hz than non-HCQ group (p=.004, <.001 respectively).

Conclusion: Otological symptoms and sensorineural hearing loss are prevalent among SLE patients. Chronic administration of HCQ may have an ototoxic effect.

REFERENCES:

- [1] Fiehn, C., et al. "Safety management in treatment with antimalarials in rheumatology. Interdisciplinary recommendations on the basis of a systematic literature review." *Zeitschrift für Rheumatologie* (2020): 1-9.

Figure 1. Otological manifestations in the study SLE patients (n=48) and the healthy controls (n=12)

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3742

POS0785

CHANGING EXPRESSION PROFILES OF LONG NONCODING RNAs, MIRNAS, MRNAS AND CIRCULAR RNAs IN LABIAL SALIVARY GLANDS OF PRIMARY SJÖGREN'S SYNDROME (PSS)

G. Feng¹, L. Huang², J. Ji³, C. Dong³, Y. Xia³, C. Cheng⁴, Z. Gu³. ¹Affiliated Hospital of Nantong University, Department of Stomatology, Nantong, China; ²Affiliated Hospital of Nantong University, Department of Critical Care Medicine, Nantong, China; ³Affiliated Hospital of Nantong University, Department of Rheumatology, Nantong, China; ⁴Nantong University, Jiangsu Province Key Laboratory for Inflammation and Molecular Drug Target, Nantong, China

Background: Primary Sjögren's syndrome (pSS) is a relatively common autoimmune disease characterized by oral and ocular dryness. An increasing number of studies have revealed that long non-coding RNA (lncRNA), miRNA, mRNA and circular RNA (circRNA) contributes to the pathogenesis of autoimmune diseases. **Objectives:** To explore lncRNA, miRNA, mRNA and circRNA expression profiles in labial salivary glands (LSGs) in pSS patients and their biological functions in the regulation of pSS.

Methods: The expression of 75,550 lncRNAs, 2,318 miRNA, 20,292 mRNAs and 6,877 circRNAs were determined in the LSG of six pSS patients and six healthy controls using microarray experiments. Validation was performed in pSS patients and controls using real-time PCR. lncRNA-mRNA co-expression and gene-pathway networks were constructed using bioinformatics software.

Results: A total of 599 lncRNAs (upregulated: 279, downregulated: 320), 78 miRNAs (upregulated: 26, downregulated: 52), 615 mRNAs (upregulated: 590, downregulated: 25) and 160 mRNAs (upregulated: 110, downregulated: 50) were differentially expressed in the LSGs of pSS patients. Five of these lncRNAs were validated using real-time PCR. lncRNA HCP5, lncRNA SNHG5, lncRNA IFI44L, lncRNA CMPK2 were significantly upregulated and lncRNA TTYH1 were downregulated in pSS. GO

and KEGG biological pathway analysis were performed to predict the functions of differentially expressed lncRNAs and co-expressed potential targeting genes. Subsequently, a ceRNA (lncRNA-miRNA-mRNA) network including 2320 ceRNA pairs was constructed based on predicted miRNAs shared by lncRNAs and mRNAs.

Conclusion: The expression profile provided a systematic perspective on the potential functions of lncRNAs, miRNAs, mRNAs and circRNAs in the pathogenesis of pSS. Therefore, this study will aid in the development of new diagnostic biomarkers and drug therapies.

REFERENCES:

- [1] Le Dantec C, Varin MM, Brooks WH, Pers JO, Youinou P, Renaudineau Y. Epigenetics and Sjogren's syndrome. *Curr Pharm Biotechnol*. 2012 Aug;13(10):2046-53.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3784

POS0786

UNMET TREATMENT NEEDS IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): A CROSS-SECTIONAL ASSESSMENT OF DISEASE ACTIVITY IN SLE PATIENTS DURING THEIR LAST VISIT

Q. Gioti¹, K. Chavatzas², G. Belevonis¹, S. Koutsovit¹, C. Katsimpari¹, I. Sofianos¹, A. Tatsi¹, P. Tzanis¹, A. Lazarini¹, K. Klavdianou¹, I. Giannakopoulou¹, E. Kalavri¹, E. Theotikos¹, A. Elezoglou¹, D. Boumpas², A. Fanouriakis^{1,2}, ¹"Asklepieio" General Hospital, Department of Rheumatology, Athens, Greece; ²"Attikon" University Hospital, Rheumatology and Clinical Immunology Unit, Athens, Greece

Background: The current goal of treatment in SLE is remission or low disease activity (LDA) and prevention of flares, achieved with the lowest possible dose of glucocorticoids. Nevertheless, in current clinical practice a significant number of patients still has active disease.^{1,2}

Objectives: To assess the current disease activity state of SLE patients during their most recent visit in two centers (Department of Rheumatology in "Asklepieio" Hospital and Rheumatology Unit in "Attikon" Hospital, both in Athens, Greece).

Methods: Cross-sectional study of patients with a diagnosis of SLE for at least one year. Patients were divided into four groups: 1) *Remission off-therapy*: SLE Disease Activity Index (SLEDAI)=0 without prednisone or immunosuppressive drugs (IS), 2) *Remission on-therapy*: SLEDAI=0, prednisone dose ≤5mg/day and/or IS (conventional and biologic, maintenance phase), 3) *LDA*: SLEDAI ≤4, prednisone dose ≤7.5mg/day and/or IS (maintenance phase), 4) *Active disease*: SLEDAI >4 and/or prednisone dose >7.5mg/day and/or IS (induction phase).² Hydroxychloroquine was allowed in all groups.

Results: 205 patients were included [95.1% female, mean (SD) age 48.4 (14.9) years and median disease duration (IQR) 6.2 (12.6) years]. A history of lupus nephritis and neuropsychiatric SLE was present in 16.6% and 17.1% of our patients, respectively, and 39% of patients had SLICC/ACR damage index (SDI) > 0. At last visit, remission off-therapy and remission on-therapy was present in 8.3% (n=17) and 15.1% (n=31) of our patients, respectively. Seventy-five patients (36.6%) had LDA, whereas 82 patients (40%) had active disease. More than 85% (86.3%) of patients were in treatment with hydroxychloroquine and 64.4% were receiving immunosuppressive drugs. Regarding glucocorticoids, 50.2% (n=103) were treated with prednisone dose ≤7.5mg/day and over 40% (42.4%, n=87) did not receive prednisone at all. A SLEDAI score 0 and 1-4 was achieved in 24.4% and 42.9% of patients, respectively, but only 3.9% had a SLEDAI > 8, indicative of high disease activity.

Conclusion: Although the majority of our patients were treated with hydroxychloroquine and glucocorticoids in acceptable levels of daily dose, four out of ten patients in our practice have active disease during their last visit. Achieving treatment goals in SLE patients remains a challenge for future novel therapies.

REFERENCES:

- [1] Fanouriakis A, Kostopoulou M, Alunno A, et al. 2019 update of the EULAR recommendations for the management of systemic lupus erythematosus. *Ann Rheum Dis* 2019; 78: 736–745.
- [2] Ugarte-Gil MF, Wojdyla D, Pons-Estel GJ, et al. Remission and Low Disease Activity Status (LDAS) protect lupus patients from damage occurrence: data from a multiethnic, multinational Latin American Lupus Cohort (GLADEL). *Ann Rheum Dis* 2017; 76: 2071–2074.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3832

POS0787

BERBERINE MODULATE LUPUS SYNDROME VIA THE REGULATION OF GUT MICROBIOTA IN MRL/LPR MICE

Y. Bao¹, J. Ji¹, Z. Xue², Z. Gu¹. ¹Affiliated Hospital of Nantong University, Department of Rheumatology, Nantong, China; ²Affiliated Hospital of Nantong University, Research Center of Clinical Medicine, Nantong, China

Background: Intestinal flora disorder and immune abnormalities have been reported in systemic lupus erythematosus (SLE) patients^{1,2}. Berberine (BBR) showed significant effects in regulating the intestinal flora, repairing gut barriers

and regulating immune cells^{3,4}. While few reports mentioned the abnormal gut microbiota and metabolites in Chinese SLE patients.

Objectives: Our investigation tried to illustrate the relationship between gut microbiota, intestinal metabolites and disease activity in Chinese SLE patients. And the effect of BBR to intestinal dysbacteriosis, multiple organ damages and over-activated immune system in MRL/Lpr mice.

Methods: 16S high-throughput (16S rRNA) sequence, qRT-PCR and gas chromatography technology were used to determine the gut microbiota and metabolites in 104 SLE patients from Affiliated Hospital of Nantong University, China. BBR was orally treated to the MRL/Lpr mice in low, medium and high doses. After 6 weeks treatment, mice were sacrificed. Serum, faeces and organs were collected for further studies.

Results: Chinese SLE patients showed higher abundance of *Bacteroidetes* and lower abundance of *Firmicutes*. The results of qRT-PCR showed high *Firmicutes/Bacteroidetes* (F/B) ratio of SLE patients. The F/B ratio was negative correlated with SLE disease activity index (SLEDA) score. Almost all the tested short-chain fatty acids (SCFAs) found statistically significant results in SLE and LN (lupus nephritis) patients, especially the propanoic acid and butyric. BBR altered the relative abundance of *Bacteroides* and *Verrucomicrobia* and the butyric acid content in colon of MRL/Lpr mice. The increase of tight junction protein also indicated the gut barrier was repaired by BBR. Treg and Th17 cells in spleen and mesenteric lymph node (MLN) were increased. These results revealed a positive therapeutic effect of berberine on SLE from gut microbiota to immune status.

Conclusion: Our study highlights current status of intestinal dysbacteriosis in Chinese patients with SLE and differences in intestinal metabolites among patients with different disease states. The regulation of intestinal flora and the repairment of gut barrier by intestinal metabolites in BBR treated mice seemed to be the factor that directed the immune responses and disease outcomes. The ultimate goal of our study was to determine the beneficial effects of regulating the gut microbiota on the treatment of SLE. The application of berberine is a relatively safe and convenient way. In the coming investigations, we plan to focus on the study of berberine and its metabolites on intestinal function and systemic immunity.

REFERENCES:

- [1] Guo, M. et al. Alteration in gut microbiota is associated with dysregulation of cytokines and glucocorticoid therapy in systemic lupus erythematosus. *Gut microbes* 11, 1758-1773, doi:10.1080/19490976.2020.1768644 (2020).
- [2] Mu, Q. et al. Control of lupus nephritis by changes of gut microbiota. *Microbiome* 5, 73, doi:10.1186/s40168-017-0300-8 (2017).
- [3] Habtemariam, S. Berberine pharmacology and the gut microbiota: A hidden therapeutic link. *Pharmacological research* 155, 104722, doi:10.1016/j.phrs.2020.104722 (2020).
- [4] Cui, H. et al. Berberine Regulates Treg/Th17 Balance to Treat Ulcerative Colitis Through Modulating the Gut Microbiota in the Colon. *Frontiers in pharmacology* 9, 571, doi:10.3389/fphar.2018.00571 (2018).

Figure 1.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3833

POS0788

CIRCULATING EXOSOMES PROMOTE LUPUS NEPHRITIS IN MRL-LPR MICE

X. Sha¹, X. Ge¹, Y. Jin¹, T. Chen¹, X. Ni¹, W. Zheng², J. Ji¹, Z. Gu¹. ¹Affiliated Hospital of Nantong University, Department of Rheumatology, Nantong, China; ²Affiliated Hospital of Nantong University, Research Center of Clinical Medicine, Nantong, China