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FRI0225

THE EULAR/ACR 2018 AND SLICC 2012 HAVE INCREASED SENSITIVITY AGAINST THE ACR 1997 CLASSIFICATION CRITERIA AND CLASSIFY NON-OVERLAPPING GROUPS OF SLE PATIENTS: SIMULTANEOUS APPLICATION ASSURES THE GREATEST CAPTURE OF PATIENTS IN CLINICAL PRACTICE

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Background: A joined EULAR/ACR initiative has proposed a new set of classification criteria for SLE based on weighted items and the use of ANA as an entry criterion.

Objectives: To compare the diagnostic performance of the old and new classification criteria against physician diagnosis in an early SLE cohort and examine phenotypic and prognostic differences among patients who are classified with the criteria.

Methods: Adult patients diagnosed by experienced physicians with SLE (n=690) or control diseases (n=301) during 2005-2016 and followed-up at least 6 months. All sets of criteria (ACR 1997, SLICC 2012, EULAR/ACR 2018) were applied. Hazard models were used to calculate elapsed time between the earliest item (of any criterion) and classification. Severity of SLE (BILAG-2004 glossary) and the SLICC/ACR organ damage index were determined.

Results: The SLICC and EULAR/ACR had increased overall sensitivity as compared to the ACR criteria (91.3%, 88.6%, 85.7%, respectively; p<0.01), especially in early-onset (<3 years) disease (91.4%, 87.3%, 79.9%, respectively; p<0.001), with comparable specificity rates (ranging 91.0–92.7%). By combining the three criteria sets, 97.1% of patients were classified. Both the EULAR/ACR and the SLICC enabled earlier SLE classification (median time-to-classification: 7.1 and 7.6 months, respectively) than the ACR criteria (median 9.1 months). Nevertheless, disease classification was delayed by >3 months in 17.3–19.9% of cases, particularly in neurological SLE (20.0–26.8%). Comparative analysis of patients who were missed by the criteria revealed significant differences in rates of individual clinical and serological features (Table 1) suggesting that existing criteria may classify non-overlapping groups of patients. Importantly, unclassified patients presented with a high prevalence of moderate/severe disease (43.3–60%) and organ damage (30–50%).

Conclusion: Despite improved sensitivity and earlier classification with the EULAR/ACR and the SLICC criteria, still SLE diagnosis may be missed or delayed even in patients with moderate to severe disease, especially neurological-dominant disease. Simultaneous application in clinical practice assures the greatest capture of patients.

Table 1. Prevalence of clinical and immunological features across groups of SLE patients who were not classified by the criteria

	Missed by the				P value
	ACR 1997	SLICC 2012	EULAR/ACR 2018	All three criteria	
	n=99	n=60	n=79	n=20	
SLICC 2012 items					
ACLE	49.5%	80.0%	72.2%	60.0%	<0.001
CCLE	10.1%	8.3%	17.7%	5.0%	0.206
Alopecia	42.4%	36.7%	63.3%	45.0%	0.008
Ulcers	12.1%	23.3%	51.9%	15.0%	<0.001
Synovitis	69.7%	86.7%	74.7%	65.0%	0.076
Serositis	6.1%	10.0%	12.7%	10.0%	0.506
Renal disorder	3.0%	3.3%	6.3%	10.0%	0.455
Neurologic disorder	8.1%	6.7%	6.3%	20.0%	0.232
Hemolytic anemia	3.0%	0.0%	2.5%	0.0%	0.503
Leukopenia	20.2%	15.0%	27.8%	10.0%	0.166
Thrombocytopenia	18.2%	6.7%	12.7%	10.0%	0.205
Anti-DNA	18.2%	3.3%	0.0%	0.0%	<0.001
Anti-Sm	2.0%	0.0%	1.3%	0.0%	0.664
Anti-phospholipid Ab	18.2%	1.7%	11.4%	5.0%	0.011
Low complement	43.4%	3.3%	21.5%	5.0%	<0.001
Coombs test	5.1%	0.0%	2.5%	0.0%	0.232
ANA	84.8%	56.7%	44.3%	50.0%	<0.001

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FRI0226

LOW EXPRESSION OF ESTROGEN RECEPTOR BETA IN RENAL TUBULAR EPITHELIAL CELL MAY CONTRIBUTE TO HYPERURICEMIA IN PREMENOPAUNTED STATES OF AMERICAL FEMALE SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: We have reported that the incidence of hyperuricemia of young female systemic lupus erythematosus (SLE) patients was higher than that of healthy young women^[1]. Whether the estrogen receptor (ER) expressed in renal tubular tissue contributes to it? There are few reports yet.

Objectives: To investigate the expression of ERs in the renal tubular cells and their relationship with serum uric acid (UA) levels in premenopausal female SLE patients.

Methods: Eighteen kidney biopsy specimens of premenopausal female SLE patients served as the lupus nephritis group (LN group), and 12 specimens of premenopausal female IgA nephropathy patients served as the IgA group. Serum UA levels and kidney index were collected, and the expression of ERs in the renal tubular epithelial cell of the two groups were determined by immunohistochemistry. According to the

percentage of the positive stained cells, the semiquantitative analysis was made. The expressions of ERs, including ER α and ER β , of the two groups were compared, and the relationship between the expression of ERs and serum UA levels were analyzed with linear regression analysis.

Results: 1. The mean ages of the LN group and the IgA group were 27.39 $\pm$ 8.09 years and 33.08 $\pm$ 5.45 years, respectively, with significantly different ($t=2.128$, $p=0.042$). There was no renal failure subject in both groups (CRE level above 120 μ mol/l), and all the SLE patients were at stage of onset.

2. Mean UA level of the LN group was significantly higher than that of the IgA group ($t=-3.149$, $P=0.004$), and the CRE level of the two groups were similar ($t=-0.109$, $P=0.914$) (table1).

3. In each group, ER β was well expressed in the tubular epithelial cells, and no in kidney glomeruli. In contrast, ER α was not expressed in the renal tissues of both groups (figure1).

4. The median score of ER β expression in the LN group was remarkable lower than that of the IgA group ($z=-2.080$, $P=0.038$, table 1).

5. Linear regression analysis indicated that ER β expression scores of the total 30 patients had significantly negative correlation with serum UA levels ($t=-2.141$, $P=0.041$, table2).

Conclusion: 1. Low expression of ER β in renal tubular epithelial cell may contribute to hyperuricemia in premenopausal female SLE patients.

2. ER α showed no expression in LN and IgA nephropathy kidney tissues.

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Table 1. Comparative analysis of main clinical biomarkers in LN groups and IgA group

	LN group (n=18)	IgA group (n=12)	P value
Age (year)	27.39 $\pm$ 8.09	33.08 $\pm$ 5.45	$t=2.128$ $p=0.042$
UA (μ mol/L)	510.33 $\pm$ 141.50	383.25 $\pm$ 78.72	$t=-3.149$ $p=0.004$
CRE (μ mol/L)	92.22 $\pm$ 11.71	91.72 $\pm$ 12.64	$t=-0.109$ $p=0.914$
ER α	0	0	
ER β	0.08(0.02,0.23)	0.20(0.10, 0.30)	$z=-2.080$ $p=0.038$

UA: uric acid; CRE: creatine; ER: estrogen receptor.

Table 2. The correlation of ER β expression scores in the renal tubular epithelial cell with serum UA levels in premenopausal female SLE patients

Variable	Unstandardized Coefficients B	Standardized Coefficients SEM	t	P	95%CI
ER β	-317.004	148.040	-2.141	0.041	-620.251 -13.757
Constant	516.455	148.040	14.641	0.000	444.198 588.712

ER: estrogen receptor

Fig 1. a. ER β expressed in renal tubular epithelial cell of LN patients; b. ER β expressed in renal tubular epithelial cell of IgA nephropathy patients; c. ER α was not expressed in renal tissue of LN patients; d. ER α was not expressed in renal tissue of IgA nephropathy patients.

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FRI0227

PREGNANCY OUTCOMES IN A LONG-TERM FOLLOW-UP COHORT OF PEDIATRIC ONSET SYSTEMIC LUPUS ERYTHEMATOSUS (PSLE) AT A TERTIARY CARE CENTER IN NORTH-WEST INDIA

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Background: Pediatric-onset SLE (pSLE) represents 10–20% of all SLE cases, and is associated with more severe disease as compared to adult onset SLE. pSLE patients are known to have more frequent systemic involvement especially related to kidneys, central nervous system and musculoskeletal system(1). Pregnant women with SLE have increased risk of adverse outcomes including disease flare, spontaneous abortion, pre-eclampsia/eclampsia, premature birth and maternal death(2). There is paucity of literature in pregnancy outcomes among women with pediatric onset SLE, especially from developing countries

Objectives: To evaluate pregnancy outcomes in a long term follow up cohort of pediatric SLE patients from a tertiary care center in North India

Methods: We have reviewed our previously published cohort of 27 pSLE patients who were diagnosed as SLE between 1998 and 2003. They were being followed-up at Pediatric Rheumatology Clinic, Advanced Pediatrics Centre, Postgraduate Institute of Medical education and research, Chandigarh, India. We have analyzed disease related complications, anti-phospholipid antibody profile, pregnancy related complications and long-term outcomes in these patients.

Results: Follow up records of 27 pSLE patients were retrieved from the clinical files. Data are available for 14 patients (i.e. 52% of the original cohort). Six (22%) of 14 patients expired due to disease related complications (2 had end stage renal disease, 1 had pulmonary thromboembolism, 2 had pulmonary hemorrhage, 2 had sepsis). Eight patients have been on follow-up till date with mean duration of follow-up of 20 years (range:16-25 years). Total patient years of follow up was 160 years. Of the 8 patients on follow up, renal manifestations were seen in 4(50%), neuropsychiatric in 4(50%), severe hematologic in 3(37.5%), musculoskeletal in 1(12.5%), anti-phospholipid antibody (APLA) positivity in 3(37.5%) patients. Disease and therapy related complications were seen in 3 patients (obesity in 2, osteopenia and avascular necrosis of femur in 1, hypertension in 1). Eight pregnancies were observed in 5 of these patients; 1 patient had primary infertility. Mean age at first pregnancy was 19 years (range: 21-25 years). All 5 patients received hydroxychloroquine throughout the pregnancy and disease activity was well controlled. APLA testing was done in 2 patients during pregnancy and both tested negative. Five live births and 3 fetal losses were observed. The fetal losses were spontaneous first trimester abortions. None had eclampsia/pre-eclampsia, ectopic pregnancy or adverse fetal outcomes (prematurity, intrauterine growth restriction, heart defects).

Conclusion: This is one of the longest follow-up studies in pSLE patients and probably the only one where pregnancy outcomes have been studied in a pediatric onset disease in context of a developing country. Our results show that in the presence of well controlled symptoms, pregnancy related outcomes are favorable with minimal fetal and maternal complications even in resource limited settings.

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FRI0228

KL-6 AS A BIOMARKER OF DEVELOPING INTERSTITIAL LUNG DISEASE IN PATIENTS WITH SJÖGREN SYNDROME

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Background: Sjögren syndrome (SS) is an autoimmune disease presented with exocrine gland inflammation and extra-glandular involvement. The