248 VALIDATION OF THE ADJUSTED GLOBAL ANTI-PHOSPHOLIPID SYNDROME SCORE IN THE ARGENTINE POPULATION

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Background Assessment of risk both for pregnancy morbidity and thrombosis in the presence of antiphospholipid antibodies (aPL) is still a challenge.

Objective to assess the performance of adjusted Global Anti-phospholipid Syndrome Score (aGAPSS) in predicting thrombosis in the setting of an external cohort study in patients with Systemic Lupus Erythematosus (SLE).

Methods Consecutive SLE patients from five rheumatology centers were included. Conventional cardiovascular risk factors were recorded as well as other underlying factors for thrombosis. Immunological tests were also recorded: ANA, anti-DNA, anti-SSA/SSB, anti-RNP, anti-Sm and aPL (Lupus Anticoagulant (LA), anti-cardiolipin (aCL) and 2 Glycoprotein I (2GPI). Medications received by patients were hydroxicloroquine, aspirin and anticoagulants. aGAPSS was calculated for each patient using a point system: 1 for arterial hypertension, 3 for dyslipidemia, 4 for LA and B2GPI and 5 for aCL. The score ranges from 0 to 17. The discriminative ability of aGAPSS was calculated by measuring the area under the receiver operating characteristic (ROC) curve (AUC). Multivariate survival analysis was performed using the proportional hazards model to identify the association of the aGAPSS cut-off value with thrombotic events adjusted to potential confounding factors. Multivariate logistic regression analysis was performed to examine the impact of multiple cardiovascular risk factors and laboratory parameters on the occurrence of thrombosis. A 95% confidence interval (CI) was selected and a p value<0.05 was considered significant.

Results Information was collected from 216 SLE patients (89.8% women, mean age at SLE diagnosis of 31 years (SD ±10.5). Ninety patients (41.6%) presented thrombotic and/or pregnancy complications. Forty-three patients (19.9%) presented at least one thrombotic episode (53 events; 28 arterial and 25 venous thromboses). Sixty women (30.9%) presented at least one pregnancy complication (81 events; 34 miscarriages, 28 fetal deaths and 19 premature deliveries). Median aGAPSS was significantly higher in patients who experienced a thrombotic event compared with those who had not [4 (IQR 1–9) versus 1 (IQR 0–5); p 0.001]. The AUC showed that aGAPSS 8 presented the best diagnostic accuracy [0.63 (CI95% 0.55–0.70) p 0.03] with 30% sensitivity and 82.5% specificity. Multivariate analysis indicated aGAPSS 8 was an independent predictor of thrombosis [OR: 2.1 (CI95% 1.03–4.12) p 0.04].

Conclusions This score is a simple tool to predict risk of thrombosis in SLE patients in daily practice. The use of aGAPSS could change the non-pharmacological and pharmacological treatment in higher risk patients to improve survival.

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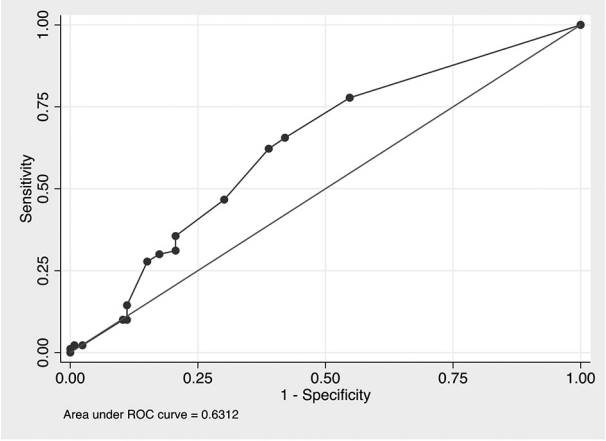
Abstract 248 Table 1 Detailed report of sensitivity and specificity

			Correctly		
Cut point	**Sensitivity**	**Specificity**	**Classified**	**LR+**	**LR-**
(≥0)	100.00%	0.00%	41.67%	1.0000	
(>1)	77.78%	45.24%	58.80%	1.4203	0.4912
(≥3)	65.56%	57.94%	61.11%	1.5585	0.5945
(≥4)	62.22%	61.11%	61.57%	1.6000	0.6182
(≥5)	46.67%	69.84%	60.19%	1.5474	0.7636
(≥6)	35.56%	79.37%	61.11%	1.7231	0.8120
(≥7)	31.11%	79.37%	59.26%	1.5077	0.8680
(≥8)	30.00%	82.54%	60.65%	1.7182	0.8481
(≥9)	27.78%	84.92%	61.11%	1.8421	0.8505
(≥10)	14.44%	88.89%	57.87%	1.3000	0.9625
(≥11)	10.00%	88.89%	56.02%	0.9000	1.0125
(≥13)	10.00%	89.68%	56.48%	0.9692	1.0035
(≥14)	2.22%	97.62%	57.87%	0.9333	1.0016
(≥16)	2.22%	99.21%	58.80%	2.8000	0.9856
(≥17)	1.11%	100.00%	58.80%		0.9889
(>17)	0.00%	100.00%	58.33%		1.0000

	ROC		Asymptotic	
Obs	Area	Std. Err.	[95% Conf. Interval]	
216	0.6312	0.0374	0.55792	0.70443



Abstract 248 Figure 1 ROC Curve

249 SPLENOMEGALY AND ANTI-NUCLEAR ANTIBODIES ARE DRIVEN BY INTERFERON- STIMULATION OF B CELLS IN LUPUS-LIKE DISEASE

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Background Systemic Lupus Erythematous (SLE) is an autoimmune disease of unknown etiology affecting 5 million people worldwide. It is known that 50%–70% of lupus patients present with an interferon-alpha (IFN-) gene signature, and it has been shown in multiple mouse models that lupus-like disease can be abolished by IFN- receptor (IFNAR) gene deficiency. Furthermore, disease can be halted by ablating the main producers of IFN-, the plasmacytoid dendritic cells. Thus, IFN- likely has a causative role in lupus-like disease.

Multiple immune cells express IFNAR, but it is not known what the effect of IFN- stimulation is on each cell type and how that stimulation affects symptom presentation. We hypothesize that BIFNAR mice would be specifically protected from splenomegaly, B cell activation, and ANA production, due to IFN-s known ability to enhance the antibody response.

Methods To examine the role of B cell responses to IFN-stimulation in mouse lupus-like disease, we studied B cell specific IFNAR-deficiency (BIFNAR) in the B6.Nba2 spontaneous lupus-like disease model, using flow cytometry, ELISA, qRT-PCR and Immunostainings. We also immunized the mice with NP-CGG or NP-Ficoll in complete Freunds adjuvant to determine the effect of IFNAR-expression by B cells during antibody responses to exogenous antigen.

Results At four months of age, BIFNAR mice displayed slightly reduced spleen sizes, although this decrease was not significant until nine months of age. Furthermore, starting at 4 months of age, BIFNAR mice displayed reduced levels of chromatin specific ANAs along with reduced populations of plasmablasts, plasma cells and activated B cells. All other measures of disease showed no difference including total IgG and IgM production, immune complex deposition and C3 complement fixation in the kidney glomeruli, and glomerular size. Somewhat surprising, antibody responses to T-dependent and T-independent immunizations were also not affected.

Conclusions IFN- stimulation on B cells contributed to splenomegaly, increased B cell activation and differentiation, and subsequent production of chromatin specific ANAs, but had no specific role in the response to exogenous antigen. Thus, IFN- remains a valid therapeutic target for SLE; especially in patients presenting with high ANAs.

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250 PREDICTION OF FETAL LOSS IN PREGNANT PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Abstract 250 Table 1 Patients' characteristics during pregnancy

Variables	Total n=338 (%)	Live birth n=300 (%)	Fetal loss n=38 (%)	P value
Characteristics				
Age (yr, mean±SD)	29.5±4.0	29.7±3.9	28.6±4.5	0.131
History of SLE (yr, mean±SD)	5.7±4.3	5.8±4.4	4.5±4.1	0.091
History of therapeutic abortion (frequency, mean±SD, range)	0.04±0.2 (0–2)	0.04±0.2 (0–1)	0.08±0.4 (0–2)	0.657
History of spontaneous abortion (frequency, mean±SD, range)	0.4±0.9 (0–7)	0.4±1.0 (0–7)	0.3±0.6 (0–7)	0.687
Region				
City	237 (70.1)	210 (70.0)	27 (71.1)	0.894
Rural	101 (29.9)	90 (30.0)	11 (28.9)	
Nullipara	291 (86.1)	258 (86.0)	33 (86.8)	0.888
Pre-pregnancy hypertension	10 (3.0)	6 (2.0)	4 (10.5)	0.016*
Unplanned pregnancy	45 (13.3)	32 (10.7)	13 (34.2)	0.000*
SLE clinical features				
Renal disorder	97 (28.7)	76 (25.3)	21 (55.3)	0.000*
Mucocutaneous	106 (31.4)	94 (31.3)	12 (31.6)	0.975
Hematologic disorder	66 (19.5)	53 (17.7)	13 (34.2)	0.015*
Neurologic disorder	5 (1.5)	3 (1.0)	2 (5.3)	0.181
Arthritis	70 (20.7)	63 (21.0)	7 (18.4)	0.712
Serositis	17 (5.0)	10 (3.3)	7 (18.4)	0.001*
Laboratory features during pregnancy				
24h-Urinary protein (g, mean±SD)	1.04±2.43	0.6±1.5	4.3±4.9	0.000*
Anti-dsDNA	261 (77.2)	226 (75.3)	35 (92.1)	0.020*
Anti-Ro/SSA	150 (44.4)	132 (44.0)	18 (47.4)	0.694
Anti-La/SSB	47 (13.9)	41 (13.7)	6 (15.8)	0.722
Anti-Sm	20 (5.9)	16 (5.3)	4 (10.5)	0.361
aPL	46 (13.6)	38 (12.7)	8 (21.1)	0.156
Hypocomplementania-C_3	90 (26.6)	62 (20.7)	28 (73.7)	0.000*
Hypocomplementania-C_4	60 (17.8)	45 (15.0)	15 (39.5)	0.000*

NOTE: *=P<0.05

Abstract 250 Table 2 Multivariable analysis of fetal loss

Variables	Risk Factors Included Individually	Risk Factors Included Simultaneously	Risk Factors Selected Using Stepwise Regression
	OR(95% CI)	OR(95% CI)	OR(95% CI)
Unplanned pregnancy	4.33 (1.71–11.00) **	3.01 (0.90–10.02)	2.84 (1.12–7.22) *
Pre-pregnancy hypertension	6.45 (1.60–26.06) **	5.24 (0.74–37.38)	-
Hypocomplementania-C_3	11.43 (5.15–25.33) **	7.09 (2.60–19.36) **	5.46 (2.30–12.97) **
Hypocomplementania-C_4	3.80 (1.81–7.98) **	0.56 (0.19–1.60)	-
Renal disorder	3.58 (1.76–7.28) **	0.33 (0.09–1.15)	-
Hematologic disorder	2.19 (1.02–4.69) *	0.90 (0.32–2.53)	-
Anti-dsDNA	3.62 (1.07–12.17) *	2.58 (0.65–10.24)	-
24h-Urinary protein			
urinary protein<0.3 g/24 hour	1	1	1
0.3≤urinary protein<1.0 g/24 hour	3.34 (1.05–10.68) *	3.23 (0.90–11.65)	2.10 (0.63–6.95)
urinary protein≥1.0 g/24 hour	14.85 (6.25–35.31) **	16.20 (3.90–67.29) **	5.89 (2.30–15.06) **

NOTE: *p<0.05; **p<0.01; Multivariable models adjusted for age at conception (continuous), history of SLE (continuous), history of therapeutic abortion (continuous), history of spontaneous abortion (continuous), region (city *vs* rural), nullipara (nullipara *vs* multipara)