SAT0203

SINGLE LAC POSITIVITY VERSUS DOUBLE AND TRIPLE POSITIVITY FOR THROMBOSIS IN SLE

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Background: The antiphospholipid syndrome (APS) is defined by the development of venous and/or arterial thromboses, and pregnancy morbidity, in the presence of antiphospholipid antibodies (aPL); lupus anticoagulant, moderate-to-high titer anticardiolipin (aCL) and anti- β 2-glycoprotein (aB2GPI). It has been suggested that the incidence of thromboembolic events were significantly higher in the triple positive subjects, and the rate of pregnancy loss was also significantly much higher in double positive subjects (1). On the other hand several studies showed that LAC is more highly associated with thrombosis risk (2).

Objectives: We aimed to investigate the risk of thrombosis in Systemic Lupus Erythematosus (SLE) patients with single LAC positivity versus double and triple positivity in Hopkins Lupus Cohort.

Methods: The Hopkins Lupus Cohort is a prospective longitudinal cohort of SLE patients ongoing since 1987. This analysis was based on cohort experience from 2003 through October 2019. Anticardiolipin and anti-Beta2 glycoprotein were defined as positive when the antibody titer exceeded 20 units. The lupus anticoagulant was determined by dilute Russell's viper venom time (dRVVT) and confirmatory mixing studies, if prolonged. It is defined as positive if a patient had a dRVVT of 45 or more second and a positive confirm ratio of more than 1.4. For each aPL, we defined the patient as positive at a given month of follow up if they ever had a positivity in previous measures. The relationships between thrombosis and aPL were adjusted for number of prior aPL assessment.

Results: There were 805 patients with a complete profile of 7 antiphospholipid antibodies, with a total of 73417 person months (6118 person years) of follow up. For any thrombosis when compared to patients with LAC positivity only, double positivity with any isotypes [1.15(0.50, 2.66) $p=0.7484$] and triple positivity with any isotypes [1.68(0.74, 3.80), $p=0.2145$] showed a higher point estimates but statistically not significant (Table 1).

Table 1. Single, double and triple positive patterns and the risk of any thrombosis.

Pattern	Number of events	Person-years	Rate per 1000 person-years	adjusted RR (95% CI)	p-value
LAC positivity only	10	633	15.8	1.00 (Ref)	
Never any aPL	33	2581	12.8	0.73(0.36, 1.47)	0.3819
any aCL positivity only	6	793	7.6	0.43(0.16, 1.18)	0.1028
any aB2GPI positivity only	7	517	13.5	0.78(0.30, 2.05)	0.6195
any aCL and aB2GPI positivity only	5	404	12.4	0.71(0.24, 2.04)	0.5211
LAC and aCL positivity	7	406	17.3	1.15(0.50, 2.66)	0.7484
LAC and aB2GPI positivity	12	490	24.5		
Triple positivity	0	147	0.0	1.68(0.74, 3.80)	0.2145

Conclusion: We found that triple or double positive aPL profiles are not superior to single LAC positivity in their association with any thrombosis in SLE patients.

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SAT0204

COMPARING OCCURRENCE AND CLINICAL SIGNIFICANCE OF ANTI-PHOSPHOLIPID AUTOANTIBODIES AMONG SUDANESE AND SWEDISH SLE PATIENTS USING CONVENTIONAL AND NATION-BASED CUTOFFS

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Table 1.

	FEIA Sudan n=92	FEIA Sweden n=291	P	PMAT/CIA Sudan n=93	PMAT/CIA Sweden n=333	P
IgA CL median/IQR	6.5/5.2	4.0/4.1	<0.0001	194/185	148/112	<0.0001
IgG CL	4.1/5.1	3.0/4.5	0.0002	205/137	190/215.1	0.09
IgM CL	2.7/6.8	3.7/5.4	0.02	214/251.5	193/350.2	0.2
IgA β 2GPI	6.3/14.2	2.7/3.8	<0.0001	212/347	118/152	<0.0001
IgG β 2GPI	4.2/2.9	1.8/2.3	<0.0001	158/110.7	145.2/147.5	0.04
IgM β 2GPI	2.0/3.0	1.4/2.2	0.006	146.2/189.7	132.5/235.4	0.09
IgA B2GP1 D1				1542/1253.5	1683/1518.1	0.045
IgA CL common cutoff n(%)	9(9.8)	17(5.8)	0.2	32(35.2)	75(22.7)	0.02
IgG CL	4(4.3)	21(6.7)	0.4	14(15)	72(22.1)	0.1
IgM CL	3(3.2)	14(4.5)	0.6	10(11.4)	43(13.1)	0.6
IgA β 2GPI	32(34.8)	43(14.9)	<0.0001	38(41.8)	76(23)	0.0004
IgG β 2GPI	10(10.9)	44(14.1)	0.4	5(5.4)	50(15.3)	0.01
IgM β 2GPI	10(10.9)	27(8.7)	0.5	12(13.6)	42(12.9)	0.8
IgA B2GP1 D1				6(6.4)	38(11.4)	0.2
IgA CL 95 th cutoff n(%)	9(9.8)	54(18.6)	0.047	36(39.6)	121(26.6)	0.6
IgG CL	8(8.7)	42(13.5)	0.2	24(25.8)	103(31.6)	0.3
IgM CL	8(8.7)	39(12.5)	0.3	16(18.2)	47(14.4)	0.4
IgA β 2GPI	18(19.6)	100(34.7)	0.006	20(22)	125(37.8)	0.005
IgG β 2GPI	2(2.1)	67(21.5)	<0.0001	19(20.4)	83(25.5)	0.3
IgM β 2GPI	14(15.22)	57(18.3)	0.5	20(22.7)	57(17.5)	0.3
IgA B2GP1 D1				25(26.9)	69(20.7)	0.2

Figure 1.

Background: Antiphospholipid antibodies (aPL) of IgA isotype are prevalent in SLE patients of African-American, Afro-Caribbean and South-African origin, but data from North Africa are lacking

Objectives: To compare and determine clinical significance of aPL isotypes in Sudanese and Swedish SLE patients using nation-based cutoffs

Methods: Consecutive Sudanese (n=115) and Swedish (n=340) SLE patients and 106 and 318 age- and sex-matched national controls were included. All patients fulfilled the 1982 ACR SLE classification criteria. IgA/G/M anti-cardiolipin and anti- β_2 GPI were analyzed with two independent assays (Fluorescence Enzyme Immuno Assay (FEIA) from Thermo Fisher Scientific and Particle-based Multi-Analyte Technology (PMAT) from Inova Diagnostics). IgA anti- β_2 GPI domain1 (D1) was investigated with chemiluminescence (CIA), Inova Diagnostics. APS-related events were obtained from patients' records. Manufacturers' 95th and 99th percentile cutoffs, based on national controls calculated by non-parametric methods, were used

Results: Sudanese patients had higher levels and prevalence of IgA aPL using manufacturers' cutoffs (Table 1 and Figure 1). IgA/IgG aPL were also higher among Sudanese controls, But, Swedish patients were more often positive for IgA anti- β_2 GPI with both assays when national cutoffs were applied (Table 1). Occurrence of IgA anti-D1 did not differ between the countries. Venous thromboses were less common among Sudanese patients and no aPL, including IgA anti- β_2 GPI associated with thrombosis in Sudanese patients. Thrombosis in Swedes associated with IgG/IgM aPL. Fetal loss associated with aPL in both cohorts most evident after national adjustments

Conclusion: IgA anti- β_2 GPI levels were generally higher among Sudanese compared to Swedish SLE patients and controls, but after national adjustments more Swedish than Sudanese patients were positive. IgA anti-D1 was not increased in Sudanese patients. Previous studies on populations of African-origin, which demonstrate high prevalence of IgA aPL positivity, should be re-evaluated using similar cutoff approach

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Figure 1. Identification of systemic lupus erythematosus (SLE) patients with bacterial infection and flare by using partial least square discriminant analysis (PLS-DA) and orthogonal PLS-DA (OPLS-DA) methods. (A) Three-dimensional PLS-DA score scatter plot, (B) the OPLS-DA score scatter plot and (C) the 'Predicted vs. Observed' plot for distinguishing bacterially infected SLE patients (green dots) from non-bacterially infected SLE patients (blue dots) based on 50 indicators. Both groups were greatly separated in the PLS-DA and OPLS-DA models. None of the non-infected SLE patients were predicted as a lupus flare.

Figure 2. Receiver operating characteristic (ROC) curves of WBC, NEUT, ESR, CRP, PCT, Treg cells, IL-6, IL-10, IFN- γ , TNF- α and their combination were drawn to identify systemic lupus erythematosus (SLE) patients with or without bacterial infection.

SAT0205

A MORE SPECIFIC INTEGRATED MODEL FOR IDENTIFYING BACTERIAL INFECTION IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a multisystemic inflammatory disorder [1]. Given that immunosuppressive therapy is adopted as the predominant treatment option for SLE, up to half of SLE patients develop infections during their disease progress, and bacterial infection serves as the leading cause of morbidity and mortality in SLE patients [2]. Owing to the therapeutic regimen to bacterial infection and SLE flare are absolutely opposite, timely diagnosis and correct treatment are of vital importance, and improper treatment strategy may be fatal. No single biomarker, however, has exhibited sufficient sensitivity and specificity to serve as a standard tool for distinguishing bacterial infection from SLE flare.

Objectives: To find a method by integrating cytokines, lymphocyte cells and routine examination biomarkers to observe its capacity for identifying bacterially infected SLE patients.

Methods: Total 175 SLE patients (65 infected and 110 flare) were recruited into our study. The criteria of bacterial infection was positive isolation of bacteria, typical clinical symptoms and signs, imaging positive results and positive feedback on antibacterial treatment and lupus flare was regarded as three points higher than their previous SLEDAI. The disease activity of SLE patients was evaluated based on Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). Lymphocyte cells (CD3⁺T, CD4⁺T, CD8⁺T, B, NK, Th1, Th2, Th17 and Treg) and cytokines (interleukin-2 (IL-2), IL-4, IL-6, IL-10, tumor necrosis factor- α (TNF- α), interferon- γ (IFN- γ) and IL-17) were measured by flow cytometry. Blood routine examination, erythrocyte sedimentation rate (ESR), C-Reactive Protein (CRP) Complement 3 (C3), C4, procalcitonin (PCT), immunoglobulin M (IgM), IgA and IgG were also evaluated. Partial least square discriminant analysis (PLS-DA) and supervised orthogonal PLS-DA (OPLS-DA) were applied to perform multivariate analysis of the data and further group the patients with bacterial infection. Receiver operating characteristic (ROC) curves were also plotted to investigate the ability of individual indicator and the combination of multiple indicators to identify bacterial infection.

Results: The PLS-DA model showed a clear identification effect by the performance of R²Y=0.991 and Q²=0.970. The OPLS-DA model (R²Y=0.996 and Q²=0.991) exhibited a better separation of patients with bacterial infection. And the Observed vs. predicted plot of the OPLS-DA model demonstrated that all SLE patients were correctly separated into infected or flare groups, indicating that the model had a strong predictive ability for bacterial infection. For single indicator, infected patients had higher WBC, neutrophil (NEUT), ESR, CRP and PCT (P=0.002, 0.019, 0.002, <0.001, <0.001, respectively), and lower Treg cells (P=0.012). The levels of serum IL-6, IL-10, IFN- γ and TNF- α (P<0.001, =0.022, 0.014, 0.011, respectively) were significantly increased in infected group. ROC curves showed that the combination of the ten indicators showed the largest AUC and the highest accuracy, as well as balanced and relatively high sensitivity and specificity. Furthermore, the AUC of the combination was greatly higher than that of WBC, NEUT, ESR, CRP, PCT, Treg, IL-6, IL-10, IFN- γ and TNF- α (P<0.001).

Conclusion: PLS-DA, OPLS-DA models including cytokines, lymphocyte cells and routine biomarkers and combination of WBC, NEUT, ESR, CRP, PCT, Treg,

biomarker	AUC (%) 95% CI	Accuracy (%)	Sensitivity(%) 95% CI	Specificity(%) 95% CI	PLR/NLR (%)	PPV/NPV (%)
WBC	0.641 (0.565-0.712)	71.43	27.69 (17.31-40.19)	97.27 (92.24-99.43)	10.15/0.74	85.71/69.48
NEUT	0.606 (0.529-0.679)	60.57	53.85 (41.03-66.30)	64.55 (54.85-73.43)	1.52/0.72	47.29/70.30
ESR	0.637 (0.561-0.708)	61.14	63.08 (50.20-74.72)	60.00 (50.22-69.22)	1.58/0.62	48.23/73.34
CRP	0.702 (0.628-0.768)	64.00	78.46 (66.51-87.69)	55.45 (45.67-64.93)	1.76/0.39	51.00/81.34
PCT	0.785 (0.717-0.843)	80.57	56.92 (44.04-69.15)	94.55 (88.51-97.97)	10.44/0.46	86.05/78.79
Treg	0.614 (0.538-0.687)	59.43	67.69 (54.95-78.77)	54.55 (44.77-64.07)	1.49/0.59	46.81/74.08
IL-6	0.682 (0.607-0.750)	70.29	49.23 (36.60-61.93)	82.73 (74.35-89.27)	2.85/0.61	62.74/73.39
IL-10	0.603 (0.527-0.676)	65.14	38.46 (26.65-51.36)	80.91 (72.31-87.78)	2.01/0.76	54.34/68.99
IFN- γ	0.611 (0.535-0.684)	54.86	80.00 (68.23-88.90)	40.00 (30.78-49.78)	1.33/0.50	44.06/77.20
TNF- α	0.616 (0.539-0.688)	68.15	56.92 (44.04-69.15)	63.64 (53.92-72.60)	1.57/0.68	48.05/71.43
Combined	0.921 (0.870-0.956)	87.43	84.62 (73.52-92.37)	89.09 (81.72-94.23)	7.76/0.17	82.09/90.74

AUC: area under the ROC curve; CI, confidence interval; PLR, positive likely ratio; NLR, negative likely ratio; PPV, positive predictive value; NPV, negative predictive value; WBC, white blood cell; NEUT, neutrophil granulocyte; ESR, erythrocyte sedimentation rate; CRP: C-reactive protein; PCT: procalcitonin; IL-6, interleukin-6; IL-10, interleukin-10; IFN- γ , interferon- γ ; TNF- α , tumor necrosis factor- α .