THU0272 VISFATIN IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: AN IMMUNE METABOLIC INTERPLAY

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Background: Visfatin is a proinflammatory cytokine (adipocytokine) that is secreted in excess from adipose tissue in obese individuals, and it has numerous metabolic and autoimmune implications: it stimulates the secretion of IL-6, IL-8, IL-10, IL-18 and TNF- α . In SLE patients these may influence disease activity and delays remission (1).

Objectives: To assess the possible effects of obesity & serum visfatin levels on SLE patients and its clinical relevance on disease process, activity and occurrence of insulin resistance.

Methods: This study was performed on 60 SLE patients satisfying the 1997 American College of Rheumatology revised criteria (ACR) and 60 apparently normal individuals with matched age and sex as control groups. All subjects were classified according to BMI into 4 groups (non-obese and obese SLE patients, non-obese and obese control persons). All patients were subjected to full history & clinical examination, assessment of SLE disease activity was done using BILAG-2004 index, laboratory investigations were done (CBC, ESR, fasting blood glucose, renal and liver function tests, lipids profile, fasting plasma insulin, calculation of insulin resistance by HOMA score, measurement of serum visfatin level by ELISA kit) and diagnosis of metabolic syndrome according to WHO definition.

Results: There were statistically significant higher grades of cardiorespiratory manifestations of BILAG score in obese compared to non-obese SLE patients. 40% of obese lupus patients were hypertensive, while only 16.6% of non-obese SLE patients. A statistically significant higher prevalence of metabolic syndrome in obese compared to non-obese SLE patients. There were statistically significant higher levels of total serum cholesterol; serum triglyceride, fasting blood sugar, fasting insulin, insulin resistance and serum visfatin; but lower level of HDL in obese SLE patients compared to non-obese SLE. The same observations were recorded on comparing non-obese SLE patients to non-obese controls & obese SLE to obese controls. A statistically significant higher level of insulin resistance and prevalence of metabolic syndrome were found among obese SLE patients when compared to obese controls and non-obese SLE patients compared to non-obese controls. Regarding serum visfatin levels obese SLE patients have significantly higher serum visfatin levels than non-obese SLE patients than obese controls than non-obese controls. In all SLE patients there were statistically significant positive correlations between serum visfatin levels and each of: BMI, waist circumference, haematological manifestations, total BILAG score of disease activity, serum triglycerides, liver functions (ALT, AST, alkaline phosphatase and total serum proteins). While a significant negative with HDL level.

Conclusions: Obesity (BMI) is an independent risk factor in SLE patients that increases the SLE disease activity and complications. Visfatin is an adipocytokine its level significantly increased in obese SLE patients & it is positively correlated with disease activity.

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THU0273 PREVALENCE AND FACTORS ASSOCIATED WITH FATIGUE IN FEMALE SLE PATIENTS AT THE HOSPITAL DEL MAR / PARC DE SALUT MAR

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Background: In patients with SLE, subjective parameters are very important as they have a great impact on the quality of life. Among them, fatigue is the most prevalent symptom in SLE, as it occurs in more than 90% of patients (1). Likewise, approximately 50% of patients consider fatigue the most disabling symptom of the disease (2). Despite its high prevalence and impact on quality of life, fatigue has not been extensively studied in patients with SLE.

Objectives: To determine the prevalence of fatigue in our cohort as well as the factors with which it is associated, its relationship with demographic variables, vitamin D levels, treatments, SLE symptoms and disease activity.

Methods: A cross-sectional study was carried out including female patients with SLE (ACR 1997 criteria) who regularly attended the Parc de Salut Mar-IMAS in Barcelona between January 2012 and May 2014. We collected sociodemographic data, vitamin D supplementation, the VAS fatigue, pharmacological treatment, main serological markers of SLE, and plasma levels of 25-hydroxy vitamin D. The association between fatigue and the different variables was evaluated by the Spearman's rho correlation coefficient for the continuous and the Mann-Whitney U test for the categorical variables.

Results: One hundred and two consecutive female patients were included. The fatigue variable was evaluated through a fatigue VAS with a mean score of 52.84 (range 0–100), a median of 59.00 and a standard deviation of 29.86. A statistically significant relationship was found between fatigue and age, MHAQ, SLICC and photosensitivity in the entirety of the 102 patients. As for the relationship between

fatigue and vitamin D insufficiency (25-OH vit. D ≤ 30 levels), the sample was divided into patients receiving vitamin D supplementation (N=60) and without supplementation (N=40), finding a significant relationship between fatigue and vitamin D insufficiency in the group without supplementation.

Table 1. Correlation between fatigue and the different SLE variables studied

Age**	Correlation coefficient	0.289
	p-value	0.003
	N	102
MHAQ**	Correlation coefficient	0.484
	p-value	0.000
	N	102
SLICC**	Correlation coefficient	0.256
	p-value	0.009
	N	102
25-OH-VitD**	Correlation coefficient)	-0.356
	p-value	0.024
	N (not supplemented)	40
Photosensitivity*	55.32 [30–80]	p-value = 0.043
	N	102

Significant value p<0.05. Med [P25–P75]. *Mann-Whitney U test; **Spearman's rho test.

Conclusions: Fatigue is highly prevalent among female patients with SLE. A statistically significant association was found between the presence of fatigue, on the one hand, and age, MHAQ, SLICC, photosensitivity, and vitamin D insufficiency in the group of patients without supplementation on the other. It is necessary to carry out further studies with a larger sample and with validated fatigue measurement scales to confirm our findings.

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THU0274 FOOTPRINTS OF NEUTROPHIL EXTRACELLULAR TRAPS ARE ELEVATED IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Impaired removal of apoptotic waste in patients with systemic lupus erythematosus-SLE has been long known as important factor that trigger autoimmune response. Neutrophil extracellular traps could be another source of autoantigens in patients with SLE.

Objectives: The aim of this study was to compare NETs markers (free DNA, myeloperoxidase) and dnase I in SEL patients and healthy controls, as well to assess their relationship with serological markers of SLE disease activity (C3 and C4 complement components, anti-dsDNA antibodies) and SLEDAI score (clinical disease activity index).

Methods: We analysed 111 sera obtained from 84 SEL patients (60 patients had 1 sample and 24 patients had 2 or 3 samples) and 50 healthy blood donors. Serum levels of myeloperoxidase, B-cell activating factor-BAFF, cell free DNA, complement components C3 and C4, antibody to dsDNA by CLIFT end ELISA assays, netolitic activity and DNase I were measured. The group of 35 patients was selected (11 with *de novo* disease) for which clinical data were recorded.

Results: SLE patients had significantly higher concentration of free serum DNA (1.69 $\pm$ 0.23 vs. 1.42 $\pm$ 0.31 ng/mL, p=0.0003), dnase I (10.4 $\pm$ 6.9 vs. 5.8 $\pm$ 5.7 U/mL, p<0.05), anti-MPO antibodies (13.8 $\pm$ 43.4 vs. 0.9 $\pm$ 0.3 U/mL, p<0.001) and myeloperoxidase activity (1607 $\pm$ 2353 vs. 560.3 $\pm$ 182.5 RU, p<0.05) in comparison to healthy controls. The ability of sera to degrade NETs was similar in both groups. Free DNA, dnase I, BAFF and anti-MPO levels as well myeloperoxidase activity showed significant correlation with anti-dsDNA antibodies measured by ELISA test. None of studied parameters showed correlation with C3 and C4 complement components. C3 and anti-dsDNA antibodies measured by indirect immune fluorescence were independent predictors of SLEDAI score in multivariate analysis, while BAFF and dnase I were significant in univariate analysis. Free cDNA was predictor of SLEDAI score higher than 7 in univariate analysis.

Conclusions: Increased amount of NETs markers found in lupus sera confirms their role in SLE pathogenesis. Determination of NETs markers could be useful serological parameter to follow disease activity in SLE patients.

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THU0275 IMPORTANCE OF SERUM TITERS OF ANTIBODIES AGAINST DOMAIN 1 OF B2 GLYCOPROTEIN 1

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Background: There is an increasing interest in the study of domain reactivity of antibodies against β 2 glycoprotein I (anti-B2GPI) in patients with antiphospholipid syndrome (APS). Antibodies targeting domain 1 of the molecule (anti-D1) as the most relevant autoantibody subpopulation. Previous information of anti-D1 B2GPI comes from APS cohorts with Caucasian, Asian, and African-American patients. However, there are no studies in Mestizo and Afro-Latin American patients.

Objectives: Our aim was to evaluate the prevalence of Anti-D1 B2GPI antibodies in a cohort of Colombian patients with systemic lupus erythematosus (SLE) with and without thrombosis, primary APS and patients with previous history of recurrent miscarriages (RM) without APS criteria.

Methods: In this cross-sectional study we measured Anti-D1 B2GPI antibodies in a group of patients from Rheumatology Department, Coagulation clinic and Recurrent Pregnancy Loss Program at the Reproduction Group at Hospital San Vicente Fundacin and Universidad de Antioquia, respectively, at Medelln, Colombia. Anti-D1 B2GPI antibodies were tested using a chemiluminescent immunoassay (QUANTA Flash B2GPI IgG, Inova Diagnostics). Mann-Whitney tests were used to compare data.

Results: One hundred and seventy seven (median age 33.5 $\pm$ 12.1 years; 89% women) patients were included. One hundred thirty eight patients had SLE (78%), 27 primary APS (15%) and 13 RM (7%). Fifty five (31%) out of 177 patients had history of thrombosis and 41 (23%) of pregnancy losses. Overall, Anti-D1 B2GPI antibodies were positive (>20 CU) in 35 (20%) of patients. Anti-D1 B2GPI were positive in 23%, 17% and 0% of patients with primary APS, SLE and RM, respectively. Overall, serum Anti-D1 B2GPI were significantly higher in patients with than without previous thrombosis (149.1 $\pm$ 336.1 vs 16.3 $\pm$ 61.8 CU, $p<0.0001$) and in patients (SLE or primary APS) with previous history of pregnancy losses (40.2 $\pm$ 123.1 vs 21.0 $\pm$ 74.5 CU, $p=0.04$). Anti-D1 B2GPI were significantly higher in patients with primary APS vs SLE with thrombosis, and in patients with SLE with thrombosis vs SLE without thrombosis (Figure). No clinical associations were found among Anti-D1 B2GPI antibodies and other APS features.

Figure 1. Mean serum levels of Anti-D1 B2GPI in a cohort of 177 patients.

Conclusions: Serum titers of Anti-D1 B2GPI antibodies were more than 9 times and 2 times higher in patients with thrombosis and pregnancy losses, respectively. In addition, serum titers were significantly higher in patients with primary APS than in SLE patients with thrombosis. Whether Anti-D1 B2GPI antibodies titers are useful to differentiate patient with primary and secondary APS requires further analysis.

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THU0276 INTERFERON-RELATED CHEMOKINE IP-10 IS A POTENTIAL BIOMARKER IN INCOMPLETE SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Incomplete SLE (iSLE) is the designation of patients who display symptoms that are typical for SLE, but with insufficient criteria to fulfil the diagnosis. Unfortunately, predictive biomarkers for SLE development are lacking. Increased IFN-type I production is an important factor in the pathogenesis of SLE. Interferon-regulated chemokines therefore could possibly be useful as biomarkers for disease progression to SLE. Candidate biomarkers IFN- γ induced protein 10 (IP-10) and monocyte chemo attractant protein (MCP-1) have shown to be increased in SLE and to correlate with disease activity.

Objectives: To determine possible candidate biomarkers IFN- γ induced protein 10 (IP-10) and monocyte chemo attractant protein (MCP-1) in patients with iSLE.

Methods: Serum samples were collected of 30 iSLE patients, 29 SLE patients, and 17 ANA-negative patients with histologically proven cutaneous lupus erythematosus (ANCL). Outcomes were compared with 25 age- and gender-matched controls (CTL) and 31 rheumatoid arthritis (RA) patients as disease control group. Levels of IP-10 and MCP-1 were measured using ELISA.

Results: IP-10 was significantly increased in SLE and RA patients compared with CTL and ANCL. IP-10 levels were increased in 23% of iSLE patients. These patients had higher SLE disease activity index (SLEDAI) and more frequently decreased C3 level and joint involvement compared to those with normal IP-10 levels. Regarding MCP-1 levels, no significant differences were found between any of the groups and no correlations with clinical markers was found.

Conclusions: Levels of IP-10, but not MCP-1, might be useful as a predictive biomarker for progression to SLE in patients with iSLE, although future prospective longitudinal analyses are needed to confirm this hypothesis.

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THU0277 REASONS FOR DEFICIENCY OF PHYSICAL INACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is associated with musculoskeletal complaints, fatigue and reduced quality of life. Physical exercise can play a crucial role in the treatment of rheumatic diseases, optimizing both physical and mental health.

Objectives: To characterize physical activity (PA) and its impact on SLE patients.

Methods: 85 SLE outpatients (92% female; age 44.2 $\pm$ 12.5; 57.5% with SLEDAI score $\leq$ 5, 42.5% with SLEDAI score $\geq$ 6) were included in this study. The following questionnaires were utilized: painDETECT, visual analog scale for pain (VAS 0 - 100 mm), short-form health survey (SF - 36, quality of life), the FACIT-Fatigue Scale and the Health Assessment Questionnaire (HAQ - DI). PA was assessed for every patient using the long form of International Physical Activity Questionnaire (IPAQ - LF) and the Metabolic Equivalent of Task (MET) minutes per week (min/wk) (physiological measurement expressing calories of physical activities). The participants were classified in 3 groups according to the PA levels conferring to the guidelines of IPAQ. Physical inactivity was defined as fewer than 150 min/week spent in moderate or vigorous physical activities. Furthermore, the patient reasons "to be not physical active" and their opinion regarding the influence of PA on disease-related symptoms (on a scale of 0-10) were obtained.

Results: 10.6% of SLE patients were physically inactive (525.2 $\pm$ 277.3 MET-Min/wk), 31.8% had a moderate physical activity, and 57.6% were physically active. Physical inactivity was associated with higher fatigue (FACIT-F, $p<0.04$) and lower "vitality" (SF-36, $p<0.03$) scores. Moreover, the subjective impact of fatigue on PA was significantly higher in physically inactive patients compared to physically active patients (the patient's score: 7.75 $\pm$ 1.25 vs. 5.5 $\pm$ 0.94, $p<0.04$). Moderate and severe pain (more than 40 mm VAS) was also associated with physical inactivity (OR 12.38, 95% CI 1.69 to 144.3, $p=0.0056$). In contrast, HAQ-DI was not related to levels of PA. Although physical inactivity correlated