impact of the birth month in the development of systemic lupus erythematosus

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Background There is evidence that most individuals with Systemic Lupus Erythematosus (SLE) have been born at the end of the winter season, mainly because of the influence of the mother’s exposure to sunlight during pregnancy, possibly affecting vitamin D metabolism. The objective was to evaluate the influence of the birth month in the development of SLE.

Methods We included consecutive patients with childhood-onset SLE (cSLE) (age at onset of disease <16 years) and adult-onset SLE (age of onset of disease >16 years) from the Rheumatology outpatient unit in Brazil. The control group consisted of volunteers no history of autoimmune disease. Through the review of medical records the patient’s date of birth was obtained and the patients were classified according to the months and seasons of the year in which they were born. The results were presented in a descriptive way and the statistical analysis was performed through the chi-square test. For all analyses p<0.05 was considered statistically significant.

Results A total of 1460 subjects (760 patients and 700 controls) were included. Of the patients analyzed, 662 (87.1%) were adult-onset SLE and 98 cSLE (12.89%). The mean age of the adult SLE was 42.4 years (SD ±12.7) and cSLE was 17.8 years (SD ±10.1). Patients who were born at the end of the winter season [n=65 (8.5%)] presented a statistically significant difference in relation to the control group [n=55 (7.8%)] (p=0.011). When it was considered only patients with cSLE, it was observed a significantly higher birth numbers of cSLE patients during the winter season in Brazil (June 21-September 21) when compared to the controls (p=0.018), and cSLE presented presented a birth frequency in winter (35.7%) twice as high as those born in summer (17.34%) and spring (17.34%). A significant difference was also observed in cSLE in the month of August (which is winter in Brazil) (p=0.042), when compared to the controls. Adult SLE had no differences with the control group in any month (p>0.05).

Conclusions It is believed that the winter season interferes with the development of SLE, especially in cSLE. These results may reinforce the idea that climate can be a contributing factor to the development of cSLE.

Funding Source(s): CNPq FAPESP

207

A HIGH GENETIC RISK SCORE IS ASSOCIATED WITH EARLY DISEASE ONSET, ORGAN DAMAGE AND DECREASED SURVIVAL IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background Systemic lupus erythematosus (SLE) is a chronic, autoimmune disease with a complex genetic etiology. Over 100 risk genes for SLE have been identified at genome-wide significance, but their overall effect on disease severity has not previously been studied. We therefore assessed the relationship between a high genetic risk score and the development of organ damage in SLE.

Methods Patients with SLE, who met 4 ACR criteria (n=1001), and healthy controls (n=2802) were genotyped using a 200K Immunochip SNP Array (Illumina). A genetic risk score (GRS) was assigned to each individual based on 57 SLE risk loci which have previously shown association (p<5×10^-8) with SLE according to Chen et al. (Curr Opin Rheumatol, 2017; 29(5):423-433), weighted by their SLE susceptibility odds ratios (ORs). Clinical data was retrieved from medical charts.

Results SLE prevalence increased with increasing GRS (figure 1A) and was higher in the highest compared to the lowest GRS-quartile (OR 12.32 (9.53–15.71) p=7.9×10^-6). SLE onset occurred 5 years earlier in the high compared to the low quartile (figure 1B). The OR for organ damage increased with increasing GRS (figure 1C) and was significantly higher in the high compared to the low GRS-quartile (OR 1.47 (1.06–2.04) p=2.0×10^-2). Moreover, patients in the high quartile had an increased prevalence of nephritis (OR 2.22 (1.50–3.27), p=5.9×10^-5), end-stage kidney disease (ESKD) (OR 5.58 (1.50–20.79), p=1.0×10^-2) and anti-dsDNA antibodies (OR 1.83 (1.92–8.1), p=5.1×10^-3), anti-cardiolipin-IgG (OR 2.16 (1.30–3.59), p=2.8×10^-3) and anti-2-glycoprotein-I (OR 1.69 (1.04–2.74), p=3.3×10^-2). Analysis of renal biopsy data showed that the prevalence of proliferative nephritis was significantly higher in the high, compared to the low, quartile (OR 2.42 (1.30–4.49), p=5.1×10^-3). Moreover, the patients in the high GRS-quartile displayed decreased survival until their first organ damage (HR 1.51 (1.04–2.25), p=3.7×10^-2), first cardiovascular event (HR 1.65 (1.03–2.64), p=2.6×10^-2), nephritis onset (HR 2.53 (1.72–3.71) p=9.6×10^-3) and ESKD (6.78 (1.78–26.86), p=6.5×10^-3). Lastly, OR for mortality increased with increasing GRS (figure 1D), with a 5 year decrease in overall survival in the high compared to the low quartile (HR 1.82 (1.04–3.19), p=2.4×10^-2).

Conclusions A high genetic risk score is associated with earlier disease onset, increased risk of organ damage and impaired