PRELIMINARY ANALYSIS OF LONGITUDINAL EVOLUTION OF ANGIOGENIC (PLGF) AND ANTIANGIOGENIC (sFlt-1) CYTOKINES SERUM LEVELS IN PREGNANT WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS WITH AND WITHOUT PREECLAMPSIA

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BACKGROUND

Most patients with systemic lupus erythematosus (SLE) develop the disease in the reproductive phase of life and pregnancy in this group has an increased risk of preeclampsia (PE). We recently demonstrated by transversal analysis that sFlt-1, VEGF, PIGF serum titers and the sFlt-1/PIGF ratio are useful for the differential diagnosis between SLE in remission, lupus nephritis and PE. The present study evaluates the longitudinal behavior of these cytokine serum levels during pregnancy in patients with SLE.

MATERIALS AND METHODS

Longitudinal analysis of sFlt-1, VEGF, PIGF serum titers during SLE pregnancy. Peripheral venous blood samples were collected at the following gestational age intervals: 16–18, 24–26, 30–32, 34–36 and 38–40 weeks. For the analysis of longitudinal evolution, the mixed regression model was used. To allow the visualization of the evolution of these values during the five visits, smooth curves were constructed using the LOWESS method (locally weighted regression).

RESULTS

Samples from 76 pregnancies were analyzed. Of these, 8 had PE and 68 did not. The mixed regression analysis of the longitudinal evolution of the serum levels of sFlt-1, PIGF and the sFlt-1/PIGF ratio demonstrated that there is a significant difference between the titles of these cytokines in the groups with and without PE (Tables 1, 2 and 3). Statistical modeling has shown that, during the pregnancy of patients who are going to have PE, serum sFlt-1 levels and the sFlt-1/PIGF ratio increase and PIGF levels decrease. These results are presented visually through the curves smoothed by the LOWESS method (Figs. 1, 2 and 3).

Table 1. Coefficients and measures of dispersion obtained in the mixed model for trajectories of serum levels of sFlt-1.

sFlt	Coefficient	p-value	95% confidence interval	
PE	4467.5	< 0.001	3306.3	5628.7
no PE	2019.6	-	1657.6	2381.5

Table 2. Coefficients and dispersion measures obtained in the mixed model for trajectories of serum levels of PIGF.

PIGF	Coefficient	p-value	95% confidence interval	
PE	-324.1	0.004	-546.8	-101.4
no PE	457.4	-	387.2	527.7

Table 3. Coefficients and measures of dispersion obtained in the mixed model for trajectories of the sFlt-1/PIGF ratio.

sFlt1/PIGF	Coefficient	p-value	95% confidence interval	
PE	114.2	< 0.001	85.8	142.7
no PE	8.3	-	- 0.52	17.2

Figure 1. Smoothed curves of the trend in serum sFlt-1 levels, stratified by PE. 0: without PE; 1: with PE.

Figure 2. Smoothed curves of the trend in serum PIGF levels, stratified by PE. 0: without PE; 1: with PE.

Figure 3. Smoothed curves of the sFlt-1/PIGF ratio trend, stratified by PE. 0: without PE; 1: with PE.

CONCLUSION

In this preliminary study, despite the small number of cases of PE, it was possible to identify that there are differences between the longitudinal curves of these cytokines of patients with SLE who will develop PE with those who will not.