PO.8.176 INFLAMMATION IN BLOOD AND PLACENTA IN SLE PREGNANCIES

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Background Adverse pregnancy outcomes, including preterm birth and preeclampsia, are more prevalent in women with SLE compared to healthy women. The immunopathological mechanisms causing these complications are largely unknown and we need methods to predict which women who are at high risk of developing them. Granulocytes are drivers of acute inflammation and have emerged as key effector cells in SLE pathogenesis. In SLE, granulocytes are activated by autoantibodies and immune complexes and granulocyte activation, identified by low CD62L expression, is associated with vascular inflammation. A particular subset of neutrophils referred to as low-density granulocytes (LDGs) was first identified in SLE and display proinflammatory characteristics compared to normal-density granulocytes (NDGs). Granulocyte activation and LDGs have not previously been studied in SLE pregnancies.

Purpose To determine whether pregnant women with SLE have increased granulocyte activation and higher proportions of LDGs in blood compared to healthy pregnant women.

Methods In this multicenter study, 44 pregnant women with SLE were included in collaboration with five Rheumatology clinics in Sweden and 20 healthy pregnant women were included at one antenatal clinic after informed consent. Clinical data related to the SLE disease and pregnancy outcome were collected. Peripheral blood samples from women with SLE and healthy women were collected in the first, second and third trimester. After density centrifugation, the proportion of LDGs among mononuclear cells and CD62L expression on LDGs and NDGs were determined by flow cytometry. Placentas were examined by one placental pathologist, blinded to the patient background.

Results The proportion of LDGs was significantly higher in all three trimesters in SLE compared to healthy pregnancies ($p=0.001$, $p=0.02$ and $p=0.003$, respectively). Both LDGs and NDGs from women with SLE displayed decreased surface density of CD62L compared to healthy women indicating increased activation (LDGs first trimester $p=0.02$, NDGs first trimester $p=0.004$ and third trimester $p=0.02$). In addition, LDGs were significantly more activated compared to NDGs in both pregnant women with SLE and healthy pregnant women. Histologic chorioamnionitis, defined by infiltration of granulocytes in the fetal membranes chorion and amnion, was present in 28% of placentas from women with SLE and in 18% of placentas from healthy women. The frequency of adverse pregnancy outcomes, including preeclampsia, miscarriage, preterm delivery, small for gestational age infant and low birth weight, was 43% among women with SLE compared to 20% among healthy women.

Conclusions We report increased granulocyte activation and inflammation in SLE compared to healthy pregnancies. Granulocyte activation may contribute to placental vascular inflammation and dysfunction, which could lead to decreased placental function in women with SLE. Prospective studies in a larger cohort including collection of postpartum blood samples are ongoing to determine whether granulocyte inflammation in blood and placenta can predict adverse pregnancy outcomes in women with SLE.

PO.8.177 LOW COMPLEMENT LEVELS IN THE FIRST TRIMESTER PREDICT DISEASE FLARE IN SLE PREGNANCY: A NETWORK META-ANALYSIS ON 532 PATIENTS

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Purpose Complement system is a key-player in the pathogenesis of systemic lupus erythematosus (SLE); its decreases correlate with disease activity and precedes flare. Since synthesis of complement proteins increase during gestational course, it is debated whether complement levels exert a prognostic role in pregnant women with SLE.

We performed a network meta-analysis to assess the prognostic role of complement in pregnant SLE women, to evaluate the possible role of complement fluctuations during pregnancies.

Methods Data from available prospective studies (Jan 2002-Dec 2020) investigating pregnancies in at least 50 SLE patients, excluding miscarriages before 12 weeks, were pooled together. After a systematic literature search, corresponding authors of 19 retrieved studies meeting inclusion criteria were invited to contribute with additional data, including complement levels [6 months before pregnancy, at conception, 1st trimester (T1), 2nd trimester (T2), 3rd trimester (T3) and 3 months after delivery].

Results A total of 532 SLE women from four eligible studies were included in the analysis.[1–4]Lupus Nephritis (LN) was diagnosed in 237 patients (44.5%) and Antiphospholipid Syndrome in 68 (12.8%). A total of 170 patients (32%) experienced a flare during pregnancy, defined as need of new Immunosuppressants or increase of prednisone > 9 mg/day.

Patients with LN had significantly lower mean levels of complement (C3 at conception; C3 at T1; C3 after 3 months of delivery; C4 at all timepoints except for C4 at T3).

SLE patients who experienced flares during pregnancy had significantly lower mean levels of complement (all timepoints