Angela Tincani and Francesca Crisafulli

The outcome of Systemic Lupus Erythematosus (SLE) pregnancies has dramatically improved over years thanks to pregnancy planning, multidisciplinary management and close monitoring. According to EULAR recommendations, pre-pregnancy counselling with the identification (and management) of possible disease-related risk factors (such as active or past lupus nephritis and presence of antiphospholipid antibodies or antiphospholipid syndrome, APS), assessment of disease activity during pregnancy (including renal function parameters, anti-dsDNA and serum C3/C4) together with obstetrical monitoring are necessary to achieve a good pregnancy outcome. A recent evaluation of our SLE pregnancy cohort recruited from 1987 to 2017 showed a number of losses not significantly different to that observed in the general obstetric population; it is of interest that all the patients enrolled received pre-pregnancy counselling and were prospectively followed during gestation by a multidisciplinary team. According to this finding, a recent paper with data derived from Norwegian Registers underlines that adverse pregnancy outcomes (APO) occur more frequently in SLE patients only in the presence of active disease. However, the data are not univocal. A recent meta-analysis still underlines the higher frequency of APO such as preeclampsia (PE), spontaneous abortion, preterm birth and small for gestational age (SGA) newborns in SLE patients. So much effort is still devoted to identify new predictors of APO and possible protective strategies.

The uterine artery Doppler applied to SLE pregnancies shows an increased mean pulsatility index while the same patients display a higher ratio of two angiogenic biomarkers (sFlt-1/PIGF) related to placental dysfunction. A more recent work shows higher levels of Pentraxin 3 (PTX3) in the general obstetric population with early-onset PE. Studying placental histology, a higher number of neutrophils and neutrophil extracellular traps (NETs) were detected in both SLE and non-SLE pregnancies with PE as compared with controls. Taken together these observations suggest that also innate immunity could play a role in the occurrence of APO observed in this condition.

Many studies have assessed the beneficial role of hydroxychloroquine (HCQ) in SLE pregnancies. The use of HCQ is associated with a lower frequency of preterm birth and intrauterine growth restriction, less disease flares and reduction of the risk of fetal loss and SGA in patients with lupus nephritis. On the other hand, the use of prednisolone was associated with lower birth weight and higher rate of preterm birth. In our cohort, the exposure to corticosteroids in doses greater than 35 mg/week in the 1st trimester was associated with preterm birth (<37 th weeks), while in the 3rd trimester with severe preterm birth (<34 th weeks). A recent study had assessed the improvement of pregnancy outcome in women with refractory obstetric APS treated with pravastatin, given the strong association between SLE and APS, this could be an interesting topic to develop in the future.

The interest in long-term outcome of children born to mother with SLE raises from few observational studies suggesting an increased risk of neurodevelopmental disorders, congenital heart defects and autoimmune diseases. However, the risk of these adverse outcomes is small, and the large majority of children are in good health. Recently, the neurodevelopmental status of 40 children (median age 7.4 years) born to women carrying antiphospholipid antibodies (with or without SLE) was investigated by child neurologists and psychiatrists. All the children resulted normally intelligent but a slight increase in the frequency of epilepsy, sleep disorders and learning disability was observed. In this respect, a recent study performed in animals pointed out the role of HCQ as protector of fetal brain development, offering a possible future preventive strategy. In conclusion, most of the young women affected by SLE can now carry out one or more pregnancies thanks to the improvement in prevention, early recognition and treatment of pregnancies complications. Nevertheless, further studies are necessary to reduce the risk of pregnancy morbidity still reported in some patients.