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Dear editor,

Pregnancy success rates in women with systemic lupus erythematosus (SLE) have improved significantly in recent years, in that pregnancy morbidity has been reduced from 40% in the early 1960's to less than 15% in recent years [1]. Pregnancy was previously discouraged in women with SLE, but the twenty-first century has brought focus on pregnancy management and in maternal and fetal outcomes and recent data suggest that women with stable SLE (if adequately treated) have favourable pregnancy outcomes with live birth rates as high as 80% [2]. In a systematic review on observational studies, Smyth et al found that in patients with SLE, both lupus nephritis (LN) and antiphospholipid antibodies (aPL) increase the risks for maternal hypertension and premature births[3].

We would like to congratulate Moroni and her team for publishing the first prospective multicentre data on maternal and fetal pregnancy outcomes in women with a history of LN [4, 5]. These data are urgently needed and provide a further piece in the puzzle towards a more complete picture in the understanding of pregnancy outcomes in women with SLE and in particular in patients with underlying LN. The only previous prospective data on women with LN focused on SLE activity after switching mycofenolate mofetil maintenance to azathioprine prior to conception [6].

Moroni et al included 61 women (59 Caucasians and 2 Asians) assessing 71 pregnancies followed from 2006-2013, who fulfilled the American College of Rheumatology (ACR) classification criteria for SLE, with a biopsy or clinically diagnosed LN and who fell pregnant in the above mentioned period attending the pregnancy clinic 3 months prior to conception. Women were closely followed up on a monthly basis.

Assessing maternal outcomes, 19.7% of the patients flared (18.3% were reported as mild and 1.7% as severe), 8.4% developed pre-eclampsia and two cases developed haemolysis and

elevated liver enzymes and low platelet count (HELLP syndrome). Predictors of maternal outcomes were SLE duration, previous renal flares and arterial hypertension, whereas significant predictors of flares were BMI, hypo-complementaemia (low C3 and C4), anti-double-stranded DNA antibodies and anti-C1q antibodies [4].

With regards to fetal outcomes, the reported live birth rate was 91.8%, and the 8.2% fetal loss rate was divided into 4.1% miscarriages (in this study defined as pregnancy loss < 20 weeks of gestation) and 4.1% stillbirths. Of the live-births, 61% were delivered at term, 30% were born pre-term and 27% had a birth weight < 2500g. All patients received aspirin. Factors associated with fetal loss were lupus anticoagulant, anti-cardiolpipin IgG, anti-βglycoprotein-I and pre-existing arterial hypertension. SLE activity, proteinuria, a history of renal flares, arterial hypertension and active LN increases the risk of preterm delivery [5].

There are three aspects of particular note with regards to fetal outcomes which supplement previous data very nicely; Firstly, that an increase in SLEDAI and proteinuria seem to increase the likelihood for preterm delivery. Albeit based on a relatively low event rate, this information was not available from previous data and might guide clinicians in their decision making in the management of these patients. Secondly, a reassuringly low rate of fetal loss was observed (in this study defined as neonatal death within 28 days post delivery). It may well be that this has been influenced by the fact that all women were treated with aspirin. Thirdly, an interesting observation was that women who were taking hydroxychloroquine (HCQ) had a significantly reduced risk to deliver a small for gestational aged baby (p=0.023). In their cohort Moroni et al reported that 54.4% of women were treated with HCQ. It would be most interesting to know if these women treated with HCQ had more favourable classes of LN, if they generally had more stable disease profiles, if HCQ was given as adjuvant therapy in addition to other immunosuppressive or anticoagulation therapy and most importantly if

these women were more likely to have persistent aPL?

HCQ is currently experiencing its 'renaissance' in the field of antiphospholipid syndrome (APS) [7] and has recently been shown to improve pregnancy outcomes in women with aPL and APS [8, 9]. Its favourable safety profile especially in regards to pregnancy and lactation makes it an interesting agent for the use in pregnancy. Latest the British Society for Rheumatology (BSR) has recommended HCQ as *'the antimalarial of choice in women requiring immune modulation in pregnancy'* [10, 11]. It would be interesting to know if HCQ in the future also will have a more substantial post in the armamentarium available for LN and prospective studies defining HCQ's role in autoimmune diseases are therefore urgently needed[7, 12].

It is worth remembering that patients included in this study were mainly Caucasian, and it may therefore be difficult to draw conclusions for all pregnant LN patients. Moreover, the team report that 21.1% of the patients had pre pregnancy LN activity (full remission was only present in 78.9%), which seems rather high given the fact that in general full disease remission is recommended for at least 6 months prior to conception [13]. Thus, pregnancy outcomes may have been even more encouraging if these cases were excluded from analysis. However, at the end of the day every clinician has experienced that real patients are not always compliant with textbook recommendations, and these data therefore provide valuable information how to gauge patients in full remission and those with mild LN activity prior to embarking pregnancy. Once more this study highlights the importance of specialist multidisciplinary teams and pregnancy counselling in women with pre-existing medical illnesses [14][15].

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