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Letter to the Editor (Other)

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Changes to expert opinion in the use of antirheumatic drugs before and during pregnancy five years after EULAR: points to consider

Rheumatology key message

- Evidence and recommendations lead to a more permissive use of csDMARDs and TNFi during pregnancy.

Dear Editor, Counselling women with inflammatory rheumatic diseases (RDs) before and during pregnancy poses challenges since the well-being of two individuals, the mother and her unborn child, has to be considered. Untreated maternal RDs are likely to result in a disease flare, which in turn can lead to an adverse pregnancy outcome [1, 2]. Therefore, the modern management of women with RDs planning a family comprises a treat-to-target concept. Evidence-based international guidelines and recommendations from EULAR 2016 and ACR 2020 help when choosing a pregnancy-compatible treatment option [1, 2]. The aim of this study was to analyse changes between the current experts' view on the use of antirheumatic drugs in pregnancy and the experts' view five years ago.

We report the results of a web-based survey evaluating the use of each medication in daily practice. The survey was sent to the previous EULAR group and attendees of the 11th International Conference on Reproduction, Pregnancy and Rheumatic Diseases in 2021. The same question and answer options were used as for the EULAR consensus in 2016 [1]. For each drug the respondent had to decide whether she/he would (1, blue) recommend the drug in the same way as if the patient was not pregnant, (2, yellow) only recommend the drug if she/he feared at least moderate or (3, red) severe disease activity in its absence, or (4, black) never recommend the drug in pregnancy.

Fifty-one participants (76.5% female, 23.5% male) from 23 countries filled in the survey, among them 13 of the 16 original EULAR 2016 task force experts (Fig. 1). Of all respondents, the great majority (90%) were physicians specialized in rheumatology with a long-term experience (57%: >10 years) in the field of pregnancy and rheumatic diseases.

Compared with the voting of the EULAR task force experts in 2016, currently more experts recommended pregnancy-compatible conventional synthetic DMARDs (csDMARDs) in the same way as if the patient was not pregnant (Fig. 1). Furthermore, the current vote showed more reluctance in recommending prednisone and NSAIDs during pregnancy as compared with the voting in 2016 (Fig. 1). This more cautious attitude towards prednisone use could be explained by recent evidence describing a dose-dependent association of prednisone use with the risk of preterm delivery [3, 4]. With regard to the prescribing pattern of NSAIDs, the possible interference with fertility as well as the risk of fetal adverse effects such as ductus arteriosus constriction and oligohydramnios in case of long-term use in the second trimester could play a role [1, 2, 5]. In addition, csDMARDs and TNF inhibitors (TNFi) have a more favourable risk–benefit profile in pregnancy than high-dose prednisone or long-term NSAIDs, declassifying the latter as second-line drugs to control disease activity.

With regard to TNFi, the availability of more safety data of these biologics in pregnancy has increased the proportion of respondents that would recommend TNFi in the same way as if the patient was not pregnant or if they feared any disease worsening in its absence (Fig. 1) [6]. Pharmacokinetic differences between TNFi with regard to their transplacental transfer might explain why respondents were more restrictive when recommending complete monoclonal TNFi (infliximab, adalimumab, golimumab) during pregnancy as compared with Fab fragments (certolizumab) and fusion proteins (etanercept) [1, 2, 7]. Different prescribing patterns of TNFi could also be due to limited long-term follow-up data of exposed infants.

For biologics other than TNFi safety data in humans are limited, yet preclinical data did not show teratogenic signals [1, 2, 8]. This translates into a more cautious use of these biologics in clinical practice. However, considering the risks of uncontrolled disease to the mother and the fetus, currently more experts than in 2016 recommended some of these biologics if they feared at least moderate disease activity in its absence (Fig. 1).

The majority of respondents never recommended drugs with a teratogenic potential or small molecules with insufficient documentation on safe use in pregnancy (Fig. 1).

Together, the current opinion on antirheumatic drugs in pregnancy reflects the updated knowledge and recommendations, with a more restrictive use of NSAIDs and prednisone on one hand and a more permissive use of csDMRDs and TNFi on the other.

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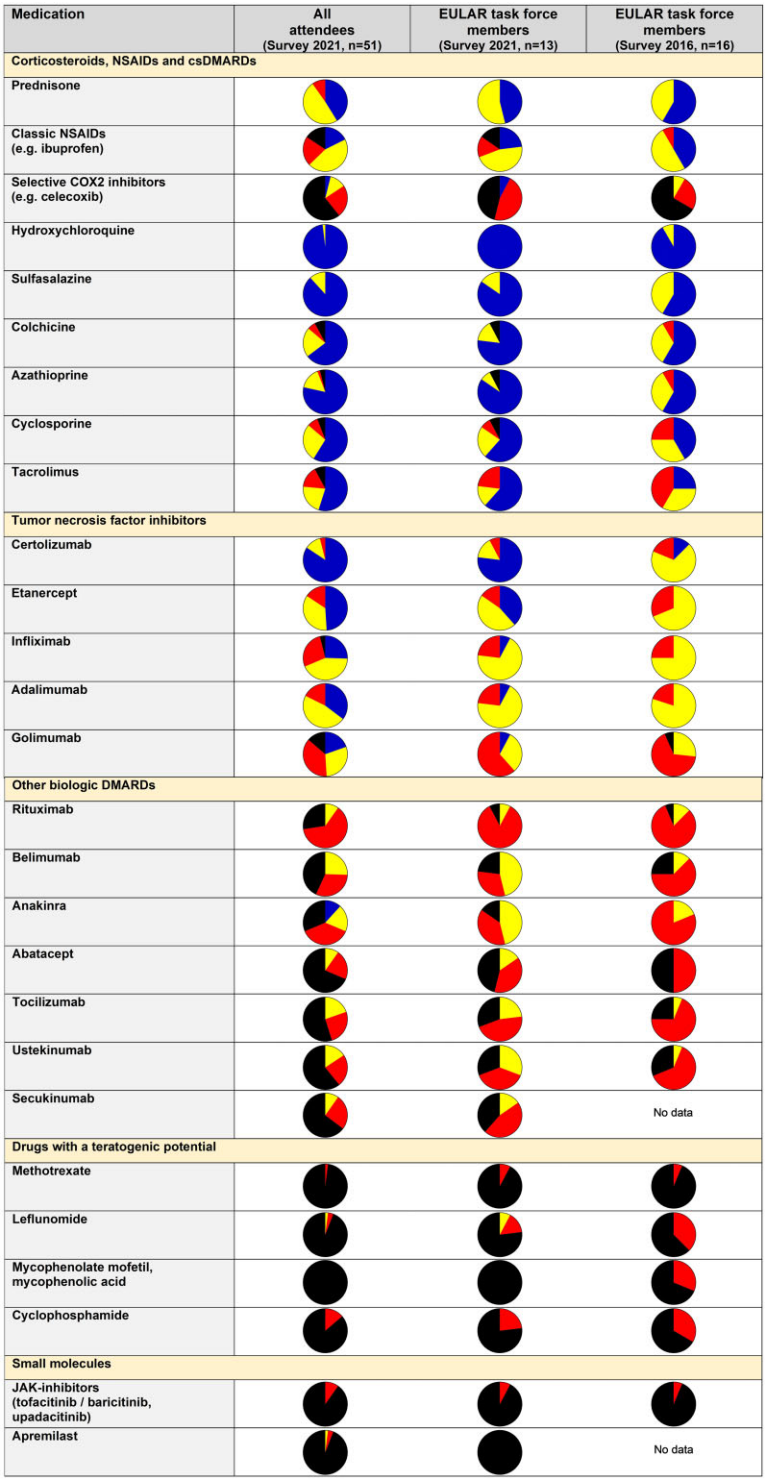
FIG. 1 Current opinion on use of antirheumatic drugs in pregnancy: conference attendees vs EULAR experts



The question for each medication was the following: what would you recommend a woman under treatment, with one of the medications above, who wants to conceive or already has a positive pregnancy test? The answer possibilities for each question were the following: – blue: I would recommend the drug in the same way as if the patient was not pregnant; – yellow: I would only recommend the drug if I feared at least moderate disease activity in its absence; – red: I would only recommend the drug if I feared at least severe disease activity in its absence; – black: I would never recommend the drug in pregnancy. In case of classic NSAIDs and selective COX2 inhibitors, the answer choices were limited to drug use in the first and second trimesters. csDMARDs: conventional synthetic DMARDs; NSAIDs: Nonsteroidal anti-inflammatory drugs.

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Data availability statement

Data are available upon reasonable request by any qualified researchers who engage in rigorous, independent scientific research, and will be provided following review and approval of a research proposal and Statistical Analysis Plan (SAP) and execution of a Data Sharing Agreement (DSA). All data relevant to the study are included in the article.

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