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Obstetric outcomes in systemic sclerosis: looking inside the sealed box.

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Dear Editor,

first of all, thank you for reviewing our manuscript and giving us advices to improve it.

We consider the topic of pregnancy outcomes in systemic sclerosis patients of crucial interest. In fact, as we stated in the letter, society has evolved and, in present years, late pregnancies are not an uncommon event, also as a consequence of improved assisted reproductive technologies. However, the topic has not been extensively assessed in the literature, and we deemed brilliant the idea of comparing the outcomes of pregnancy in systemic sclerosis patients to those of patients with other autoimmune diseases such as systemic lupus erythematosus, idiopathic inflammatory myositis, and Takayasu arteritis. However, the relevance of the topic needs a solid methodology, and we thought it would have been important to highlight some pitfalls of the aforementioned study.

We are thankful for the reviewer's suggestions and pleased to revise our manuscript according to them.

Reply to Reviewer #1:

1. I suggest that the authors include a more reflective title.

We changed the title according to your suggestion. Moreover we added a paragraph at the end of the manuscript to better explain the new title.

2. While disease controls were used, matching based on age or other variables that could associate with outcome would have enhanced the validity of the comparisons.

Even though we are aware that, using an historic cohort, matching would had been hard to achieve, we added a paragraph in the first page to address this issue.

Thank you.

Best regards.

The authors.

Giuseppe Barilaro
Carlo Della Rocca
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Obstetric outcomes in systemic sclerosis: looking inside the sealed box.

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Obstetric outcomes in systemic sclerosis: looking inside the sealed box.

To the editor,

We read with great interest the article “Poor maternal and foetal outcomes in women with systemic sclerosis: an interview-based study at a tertiary centre” by Kharbanda et al [1]. It is the first study comparing the maternal and foetal outcomes in women with systemic sclerosis (SSc) to those of patients with systemic lupus erythematosus, idiopathic inflammatory myositis, and Takayasu arteritis. Moreover, the study analyzed the outcomes of pregnancies before and after disease onset. In our opinion, certain points need clarification. First of all, patients’ data were collected by phone call, filling up a case record form. It is not the first study using this strategy [2–4], and, as the authors stated in the discussion, this bias was reduced by reviewing obstetric records shared by WhatsApp or email. However, they did not specify how many patients have sent this information, if all or part of them. **Second, the authors do not mention if the different groups were matched based on age or other clinical variables. We are aware that, using an historic cohort, matching would had been hard to achieve, but it would have improved the strength of results.** Moreover, only 15 pregnancies occurred after SSc onset and, with such a small number, results must be interpreted with caution. For instance, spontaneous abortions occurred in three out of 15 conceptions after SSc onset, but it is not specified if other causes, such as chromosomal abnormalities, had been excluded. Society has evolved and, in present years, late pregnancies, after 40 years of age, are not a sporadic event. Moreover, progressive improvement in assisted reproductive technologies, had notably increased such contingency also in couples with fertility issues. We completely agree with the authors that pregnancies in SSc patients should be considered as high-risk and therefore followed in specialized multidisciplinary units. Moreover, as the authors stated in the discussion, a large prospective

collaborative multi-centre study assessing the maternal and foetal outcomes in pregnancies of women with SSc is warranted. For instance, a large, multi-centre, prospective observational study of pregnancy in SSc (International Multicentric Study on PREgnancy in Systemic Sclerosis, IMPRESS 2) is currently ongoing and definitive results are awaited [5]. Without a solid methodology, drawing conclusions about the effect of systemic sclerosis on pregnancy and vice-versa is like doing a Schrödinger's cat experiment: you cannot infer that the cat is dead or alive until you open the box.

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