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Insights into pregnancy risks associated with active juvenile idiopathic arthritis

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Dear Editor

The study by Götestam Skorpen et al. (1) represents a significant contribution to our understanding of how juvenile idiopathic arthritis (JIA) affects pregnancy outcomes. By leveraging a robust dataset from Norwegian registries, the authors effectively address a critical gap in the literature regarding the implications of active JIA during pregnancy. However, while the strengths of the study are commendable, there are limitations that warrant further discussion.

This study demonstrates that women with active JIA face a significantly higher incidence of preterm birth, recorded at 17.6%, compared to a rate of 4.9% among control participants. This finding aligns with previous research conducted by Remaeus et al. (2) and Smith et al. (3). Notably, there were no reported cases of preeclampsia in either the active or inactive JIA cohorts, which corresponds with studies by Förger et al. (4) and García-Fernández et al. (5), despite earlier literature suggesting a potential elevated risk. Additionally, the study identified heightened rates of gestational hypertension in both active (7.2%) and inactive JIA groups compared to controls (1.7%), consistent with findings from Drechsel et al. (6) and Mohamed et al. (7). There were no significant differences in abnormal fetal growth between the JIA and control groups, supporting earlier studies by Remaeus et al. (2) and Chen et al. (8). The current research highlights the significant impact of disease activity in JIA, indicating that active JIA is associated with an increased risk of certain adverse pregnancy outcomes. Conversely, inactive JIA does not exhibit the same level of risk. This conclusion is corroborated by prior studies that suggest improvements in the management and treatment of JIA during pregnancy may have favorably affected these outcomes.

One of the primary strengths of the study is its large sample size, which enhances the reliability and generalizability of the findings within the Norwegian context. This allows for more confident conclusions to be drawn about the differences in pregnancy outcomes between women with active JIA and healthy controls, as well as those with inactive disease. The clear objectives focused on specific adverse outcomes—such as preterm birth and gestational hypertension—provide a structured framework for the analysis, making it easier for healthcare providers to understand the risks involved.

The inclusion of disease activity assessments using the Disease Activity Score with CRP (DAS28-CRP-3) during the second and third trimesters is particularly noteworthy. This suggests that the researchers are mindful of the variability of disease activity throughout

pregnancy and its potential effects on outcomes. However, the limitation regarding the lack of early pregnancy disease activity assessment could be significant. Many factors that contribute to pregnancy complications may be influenced by the disease status in the first trimester, which can set the stage for how the pregnancy will progress. This aspect raises questions about the timing of interventions and monitoring for women with JIA to optimize outcomes.

Furthermore, the absence of an analysis of JIA subtypes is another notable limitation. JIA encompasses several subtypes, each with distinct characteristics and disease courses. Understanding how these differences influence pregnancy outcomes could guide personalized management plans for expecting mothers with JIA. Without this analysis, the study may overlook critical nuances that could alter interpretation and recommendations for different patient groups.

The authors' study on JIA in adults highlights significant limitations, particularly in assessing disease activity. Concerns arise over the validity of the DAS28-CRP-3 for adult JIA populations, especially regarding potential misclassification of disease activity and its implications for treatment decisions. The absence of disease activity evaluations during early pregnancy is also critical, as hormonal changes can greatly affect disease behavior. Furthermore, the study fails to distinguish between JIA subtypes, such as polyarticular and oligoarticular JIA, which have unique clinical characteristics and treatment responses. Addressing these issues in future research is vital for improving understanding and care for women with JIA during pregnancy.

The researchers highlight increased risks of preterm birth and gestational hypertension, while their findings on preeclampsia and fetal growth are intriguing. It is surprising that women with active JIA do not exhibit a higher risk for preeclampsia, given the known links between chronic inflammation and pregnancy-related hypertensive disorders. This finding warrants further investigation, as it may point to protective factors in the JIA population or reveal the complex relationship between inflammation and pregnancy physiology. However, a significant limitation of the study is its reliance on the Medical Birth Registry of Norway (MBRN) for identifying JIA cases through ICD-10 codes, which can lead to inaccuracies. Misclassifications may arise from coding errors, diagnostic criteria variations, or differences in clinical practices, potentially skewing the prevalence of JIA and its maternal and neonatal outcomes. The ICD-10 system may overlook nuanced aspects of JIA, particularly in ambiguous cases or those overlapping with other rheumatic diseases, potentially excluding true JIA patients and distorting results. The timing of diagnosis is also crucial; if JIA is identified post-pregnancy registration, vital data may be missing from MBRN, creating gaps in understanding its effects on pregnancy outcomes. The authors' failure to address this limitation could lead to an overestimation of the study's implications regarding JIA and pregnancy, suggesting that a thorough discussion of ICD-10 coding inaccuracies would bolster the study's credibility and provide insights for future research on rheumatic diseases in pregnancy contexts.

Lastly, while the study is well-designed within Norway's healthcare framework, its generalizability to other populations is

uncertain. Differences in healthcare systems, access to care, and cultural attitudes toward managing chronic diseases during pregnancy may affect outcomes in varying contexts. Therefore, caution is recommended when extrapolating these findings to women with JIA in other countries.

In conclusion, the study by Göttestam Skorpen et al. adds to the growing body of literature regarding JIA and its implications for pregnancy outcomes. It underscores the vital role of active disease management during pregnancy for improving maternal and fetal health. However, the limitations discussed reveal areas for further research that could enhance our understanding and inform clinical practice. Additional studies that focus on early disease activity assessment, subtype differences, and international comparisons will be essential for developing comprehensive care strategies for pregnant women with JIA.

Author contributions

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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References

1. Skorpén CG, Lydersen S, Salvesen KÅ, Wallenius M. Preterm birth, preeclampsia, gestational hypertension and offspring birth weight in women with active juvenile idiopathic arthritis and healthy controls. *Front Lupus*. (2024) 2:1375857. doi: 10.3389/flupu.2024.1375857
2. Rømaes K, Johansson K, Askling J, Stephansson O. Juvenile onset arthritis and pregnancy outcome: a population-based cohort study. *Ann Rheum Dis*. (2017) 76:1809–14. doi: 10.1136/annrheumdis-2016-210879
3. Smith CJF, Förger F, Bandoli G, Chambers CD. Factors associated with preterm delivery among women with rheumatoid arthritis and juvenile idiopathic arthritis. *Arthritis Care Res (Hoboken)*. (2019) 71:1019. doi: 10.1002/acr.23730
4. Förger F, Bandoli G, Luo Y, Robinson L, Johnson DL, Chambers CD. No association of discontinuing tumor necrosis factor inhibitors before gestational week twenty in well-controlled rheumatoid arthritis and juvenile idiopathic arthritis with a disease worsening in late pregnancy. *Arthritis Rheumatol*. (2019) 71:901–7. doi: 10.1002/art.40821
5. García-Fernández A, Gerardi MC, Crisafulli F, Filippini M, Fredi M, Gorla R, et al. Disease course and obstetric outcomes of pregnancies in juvenile idiopathic arthritis: are there any differences among disease subtypes? A single-centre retrospective study of prospectively followed pregnancies in a dedicated pregnancy clinic. *Clin Rheumatol*. (2021) 40:239–44. doi: 10.1007/s10067-020-05404-w
6. Drechsel P, Stüdemann K, Niewerth M, Horneff G, Fischer-Betz R, Seipelt E, et al. Pregnancy outcomes in DMARD-exposed patients with juvenile idiopathic arthritis—results from a JIA biologic registry. *Rheumatology (Oxford)*. (2020) 59:603–12. doi: 10.1093/RHEUMATOLOGY/KEZ309
7. Mohamed MA, Goldman C, El-Dib M, Aly H. Maternal juvenile rheumatoid arthritis may be associated with preterm birth but not poor fetal growth. *J Perinatol*. (2016) 36(4):268–71. doi: 10.1038/jp.2015.193
8. Chen JS, Ford JB, Roberts CL, Simpson JM, March LM. Pregnancy outcomes in women with juvenile idiopathic arthritis: a population-based study. *Rheumatology (Oxford)*. (2013) 52:1119–25. doi: 10.1093/rheumatology/kes428