



# Commentary on the factors with liver fibrosis in rheumatoid arthritis patients treated with methotrexate

Difeng Chen<sup>1</sup> · Junwu Zhang<sup>2</sup>

Received: 17 January 2024 / Revised: 17 January 2024 / Accepted: 29 January 2024 / Published online: 23 February 2024  
© The Author(s), under exclusive licence to International League of Associations for Rheumatology (ILAR) 2024

Dear Editor

We read Slouma's paper [1] with great interest. In this paper, the author aims to determine the frequency of liver fibrosis in rheumatoid arthritis patients treated with methotrexate and to identify its associated factors. Then they found that cumulating more than 3 g of methotrexate was associated with liver fibrosis in rheumatoid arthritis (RA) patients. Having a metabolic syndrome, hypoalbuminemia, higher age, and elevated alkaline phosphatase levels were also likely to be independently associated with liver fibrosis. Despite definite results, in this letter, we raise some concerns about some of the details in the article.

In this study, we noted that 20 factors were analyzed for the univariate logistic regression analysis to analyze the factors associated with liver fibrosis in RA patients treated with methotrexate, which included age  $\geq 60$  years, male gender, alcoholic consumption, BMI  $\geq 25$ , abnormal WC, comorbidities, metabolic syndrome, disease duration  $\geq 10$  years, erosive disease, positive RF, positive ACPA, DAS28 CRP  $> 2.6$ , DAS28 ESR  $> 2.6$ , ESR  $> 20$  mm, CRP  $> 8$  mg/l, presence of fatty liver, steroids use, cumulated dose of MTX  $> 3$  g, hypoalbuminemia, increased ALP, and increased AST. However, these 20 factors were all included in the univariate analysis for a total of 68 RA patients, and only 9 RA patients had liver fibrosis. However, the sample size of univariate and

multivariate linear regression analysis is at least 15 times that of the analyzed variable factor [2, 3]. The more variable factors are analyzed, the more example sizes are required. Therefore, more sample sizes are required to make the univariate logistic regression analysis in this liver fibrosis in RA patients treated with methotrexate. Without considering this important point, it could result in unreliable results.

Despite these comments, we extend our congratulations to Slouma et al. for their outstanding work.

**Funding** None.

## Declarations

**Ethical approval** Not applicable.

**Consent from all authors** All authors reviewed this manuscript and agreed to submit this manuscript.

**Disclosures** None.

## References

1. Slouma M, Lahmar W, Mohamed G, Dhrif O, Dhahri R, Bellali H, Gharsallah I, Ebdelli N (2023) Associated factors with liver fibrosis in rheumatoid arthritis patients treated with methotrexate. *Clin Rheumatol*. <https://doi.org/10.1007/s10067-023-06847-7>
2. Yadav SK, Singh S, Gupta R (2019) Univariate logistic regression: theoretical aspects. In: Yadav SK, Singh S, Gupta R (eds) *Biomedical statistics : a beginner's guide*. Springer Singapore, Singapore, pp 219–222. [https://doi.org/10.1007/978-981-32-9294-9\\_28](https://doi.org/10.1007/978-981-32-9294-9_28)
3. Ranganathan P, Pramesh CS, Aggarwal R (2017) Common pitfalls in statistical analysis: logistic regression. *Perspect Clin Res* 8(3):148–51. [https://doi.org/10.4103/picr.PICR\\_87\\_17](https://doi.org/10.4103/picr.PICR_87_17)

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

This comment refers to the article available online at <https://doi.org/10.1007/s10067-023-06847-7>.

✉ Junwu Zhang  
84962362@qq.com

<sup>1</sup> Department of Clinical Laboratory, Yuyao People's Hospital of Zhejiang Province, Ningbo, Zhejiang, China

<sup>2</sup> Department of Clinical Laboratory, Wenzhou TCM Hospital of Zhejiang Chinese Medical University, 9 Jiaowei Road, Wenzhou 325000, China