Letter to the Editor

Access this article online
Quick Response Code:

Website:
https://eurasianjpulmonol.org
DOI:
10.14744/ejp.2026.27672

Methodological considerations on the association between eosinophilia and tuberculosis treatment duration

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Dear Editor,

We read with interest the article by Yayla et al.,[1] entitled "The impact of eosinophilia on treatment duration in patients with newly diagnosed drug-sensitive pulmonary tuberculosis.". The authors address a relatively unexplored question; however, several methodological issues may affect the interpretation of the association between eosinophilia and treatment duration.

First, although the introduction describes eosinophilia and its possible antimycobacterial effects, the clinical rationale for why peripheral eosinophilia might influence tuberculosis treatment duration could be clearer.[2] Conversely, the operational definitions of eosinophilia, particularly the absolute eosinophil count (AEC) threshold of ≥500 cells/μL, are discussed extensively in the introduction, although these would more appropriately belong in the Methods section.

The exclusion of patients with AEC ≥1500 cells/μL deserves consideration. Patients with more pronounced eosinophilia may represent an important eosinophilic phenotype; excluding them may introduce selection bias and limit generalizability. Moreover, categorizing eosinophilia solely as present or absent using a threshold of 500 cells/μL may result in the loss of relevant information. In addition to categorical analysis, AEC could have been evaluated as a continuous variable using baseline, peak, or changes during treatment to assess a possible dose-response relationship between eosinophil levels and treatment duration.

Similarly, treatment duration was dichotomized as ≤6 months versus >6 months for logistic regression. Although clinically intuitive, this approach discards information on actual treatment duration, which ranged from 6 to 9 months in both groups. Retaining treatment duration as a continuous or time-based outcome could provide additional information and avoid the limitations associated with dichotomization.

Potential confounding is also important. Treatment duration in pulmonary tuberculosis may be influenced by disease severity and treatment response. However,

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Received: 24-08-2026
Accepted: 27-08-2026
Published: 21-09-2026

How to cite this article: Erinç A. Methodological considerations on the association between eosinophilia and tuberculosis treatment duration. Eurasian J Pulmonol 2026;28:227-228.

Table 1 does not include radiological parameters such as cavitation, bilateral involvement, or overall radiological extent. Microbiological indicators that may influence treatment prolongation are also not presented. The authors acknowledge the absence of baseline cavitary disease as a limitation. Nevertheless, because radiological severity may directly influence treatment duration, the lack of adjustment for these variables may substantially affect the observed association with eosinophilia.[3]

Baseline characteristics could also be presented more comprehensively. Sex, despite differing significantly between the groups, is absent from Table 1. Several comorbidities included in the regression model are reported only in the text. Total bilirubin and other laboratory parameters relevant to treatment tolerability and duration are also not presented. A more complete baseline table would facilitate the assessment of group comparability and residual confounding.

Finally, although the results refer to univariate analysis, the complete results and criteria for multivariable variable selection are unclear. Age was excluded because it was not significant in the univariate analysis and was similarly distributed between the groups. Relying predominantly on univariate statistical significance may overlook clinically relevant confounders. Providing the full univariate analysis and a clearer explanation of the prespecified or clinically based variable-selection strategy would improve the transparency of the regression analysis.

In conclusion, the association between eosinophilia and shorter tuberculosis treatment duration is intriguing. However, possible selection bias resulting from the exclusion of marked eosinophilia, dichotomization of eosinophilia and treatment duration, incomplete adjustment for radiological and clinical determinants of treatment duration, and limited reporting of the regression strategy should be considered when interpreting the findings. Further analyses treating eosinophil count as a continuous variable and incorporating major determinants of tuberculosis disease severity would strengthen the conclusions.

Conflicts of Interest

The authors have no conflicts of interest to declare.

Funding

The authors declared that this study received no financial support.

Use of AI for Writing Assistance

No use of AI-assisted technologies was declared by the authors.

Author Contributions

Concept – A.E.; Design – A.E.; Supervision – A.E.; Resource – A.E.; Materials – A.E.; Data Collection and/or Processing – A.E.; Analysis and/or Interpretation – A.E.; Literature Review – A.E.; Writing – A.E.; Critical Review – A.E.

Peer-review

Externally peer-reviewed.

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