

– LETTERS TO EDITORS –

Comments on Antiphospholipid Antibodies in Non-Hodgkin's Lymphoma

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We have read with great interest the article by Buruiana et al. in Documenta Haematologica titled “Antiphospholipid Antibodies in Non-Hodgkin's Lymphoma.” This prospective, descriptive cross-sectional study analyzed 161 de novo NHL patients from the Republic of Moldova, exploring the prevalence and significance of antiphospholipid antibodies (aCL, anti- β 2GPI, and LA) in relation to lymphoma subtype, stage, age, and disease onset. The authors report a 16.2% seropositivity rate, with a trend toward antibody negativity following first-line treatment. These findings contribute to the growing literature on immune dysregulation and thrombophilic states in hematological malignancies, especially B-cell NHL [1].

While the study provides useful information, it has significant methodological shortcomings that deserve to be addressed constructively. First, no sample size or power estimate was supplied. Bacchetti emphasizes that a lack of statistical power rationale can compromise confidence of clinical findings, particularly when dealing with subgroups or unusual outcomes. [2]. Secondly, while the authors stratify the results by demographic and clinical characteristics, they only use basic statistical comparisons (for example, chi-square tests). The lack of multivariate regression limits the capacity to adjust for potential confounders like age or NHL subtype, which may mask authentic correlations. [3].

The way inclusion and exclusion criteria are handled is another concern. There is minimal information on exclusion criteria such as past thrombotic events, autoimmune disorders, or medication history, all of which could affect antibody levels and skew results, even though patients were included based on age and consent. According to Concato et al., poorly specified study populations impair reproducibility and lower internal validity [4].

Additionally, the study did not explain blinding practices during antibody assessment or how missing data were handled. According to methodological literature, observer bias could affect how antibody tests are interpreted in the absence of blinding. [5]. The authors also omit confidence intervals for key outcomes, which are essential for gauging the precision and clinical relevance of estimates, particularly in smaller cohorts [6]. The interpretation of longitudinal changes in antibody positivity is intriguing but constrained by the small number of follow-up observations and the lack of a defined protocol for antibody retesting. Studies such as that by Jakobsen et al. stress the importance of predefined follow-up intervals and appropriate missing data strategies to ensure robust longitudinal inferences [7].

In conclusion, while Buruiana et al. offer important insights into the seroepidemiology of antiphospholipid antibodies in NHL, future research should incorporate power analyses, apply multivariate statistical methods,

and improve transparency in methodology—particularly regarding blinding, missing data, and inclusion/exclusion criteria. Standardized follow-up and broader patient

characterization would strengthen causal inferences and inform the clinical relevance of antibody testing in NHL.

References

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Clarifications

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Dear editorial staff and colleagues from Saidu Medical College

I am deeply grateful for the comments submitted. Our study is much more extensive, encompassing many more analysis criteria, and only single data obtained are reflected in this article.

No blinding study was planned from the start.

To avoid and prevent erroneous deductions regarding the proposed objectives and ensure the representativeness of the data, the calculation of the representative batch for the required level of precision, the level of confidence and the estimated proportion of the attribute present in the population was carried out by applying Cochran's formula. The decision belonged to the biostatisticians.

$$n = d[\tilde{\pi}(1-\tilde{\pi})] * (z\alpha/w)^2$$

d – design-effect = 2

$$\tilde{\pi} = 0.055$$

n – representative sample volume.

According to statistical data, the share of patients in the general population who have anticardiolipin antibodies according to bibliographic sources is on average 5%.

$$z\alpha = 1.96$$

w – the work will be carried out based on the evaluation of frequencies and their arrangement by relative values, we need the confidence interval, ES=0.05

$$n = 2 * [0.05 * 0.95] * (1.96/0.05)^2 = 145,98$$

and the 10.0% non-response rate for the research, 161 respondents are required, respecting the inclusion and exclusion criteria.

Absolutely logically, among the exclusion criterias will be found:

1. Patient age < 18 years (we only studied adult patients, and in our country it is from the age of 18)
2. Patient refusal to participate in the study
3. Presence of other comorbidities with possible association with the synthesis of anticardiolipin antibodies (rheumatic diseases, COVID-19, infections, cancers...)
4. Lack of possibility of recording patient dynamics (death, abandonment of treatment, treatment in other institutions, abroad)

95% CI - confidence intervals are represented within the statistical analysis.

We are open to collaboration.