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LETTER TO THE EDITOR

Aspartate aminotransferase in COVID-19: A probably overrated marker

To the Editor,

We read with interest the update by Spearman et al[1] discussing liver involvement in COVID-19. The review mentioned some results about liver enzymes derived from published studies, discussing the frequently reported association of aspartate aminotransferase (AST) increase with in-hospital mortality risk. This information is potentially relevant for guiding patient care and permitting early identification of subjects at high risk of death, its practical implication being, however, compromised by the fact that no studies discussed how pre-analytical, analytical and post-analytical aspects of laboratory measurements may influence obtained data and their interpretation. Issues such as the lack of standardization of commercial assays towards available international reference measurement systems (eg for aminotransferases, assays with or without the addition of pyridoxal-5-phosphate coenzyme are available on the market, providing different results),[2] the use of upper reference limits (URL) derived from protocols of unknown robustness for defining enzyme increases,[3] and the unavailability of information about management of results potentially affected by common interferents (eg AST measurements are significantly impacted even when serum samples are slightly haemolysed), all may compromise results obtained in primary studies and make their interpretation ambiguous.

Given the uncertainty of accuracy of published data, we recently examined a large cohort of COVID-19 patients admitted in our academic hospital in Milan, one of the two Italian reference centres for infectious diseases, for defining sources and clinical significance of AST increases, paying attention to all aspects of total examination process.[4] First, we found AST more frequently increased in COVID-19 patients than in previous studies: 69% of subjects displayed AST values higher than URL, much more than the pooled prevalence of 19% reported in Spearman's review.[1] The pathogenetic mechanisms for abnormal AST frequently present in COVID-19 were likely multifactorial in origin (possibly a combination of hypoxia, hyperinflammation and drug toxicity), having liver and muscles as primary sources in an approximate 60%-40% proportion. More importantly, our data failed to demonstrate an independent association of AST increases with poor outcomes, such as death and intensive care unit admission during hospitalization, as opposed to biomarkers with a strong and widely confirmed prognostic power, such as lactate dehydrogenase and serum albumin.[5]

In conclusion, after having carefully controlled all laboratory sources of variation, we were unable to confirm what other authors have published about the value of AST in COVID-19 as independent prognostic factor. Although quite frequent, AST elevations are probably a disease nonspecific epiphenomenon and have minimal clinical significance.

CONFLICT OF INTEREST

None.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were generated.

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