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LETTER TO THE EDITOR

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Serum prealbumin values predict the severity of coronavirus disease 2019 (COVID-19)

To the Editor,

Serum prealbumin assessment is a highly valuable and effective strategy for predicting disease progression in critically ill patients, as well as in those affected by chronic disorders and malnutrition.[1] Reliable evidence has also been published that serum prealbumin values are decreased in patients with coronavirus disease 2019 (COVID-19), and that its measurement may hence be clinically meaningful for early triage of these patients,[2] so that its role in predicting critical illness and unfavorable outcomes deserves deep scrutiny. We, hence, carried out a literature search, for identifying clinical studies that measured serum prealbumin in COVID-19 patients and correlated the values of this nutritional biomarker with disease severity.

We accessed the three most widely used scientific databases (PubMed, Scopus, and Web of Science),[3] using the keywords "coronavirus disease 2019" OR "COVID-19" AND "prealbumin" in all fields, with no date or language restrictions. The title, abstract, and full text of all documents identified with these search criteria were carefully analyzed, and those describing serum prealbumin values in COVID-19 patients with or without severe illness were selected. The reference list was also hand-searched, with the purpose of identifying other potentially eligible studies. A meta-analysis was finally performed, with an estimation of weighted mean difference (WMD), along with a 95% confidence interval (95% CI), of prealbumin values in COVID-19 patients with or without severe disease. When the mean value and *SD* were not evidently reported, these measures were extrapolated using sample size, median, and range, as proposed by Hozo et al.[4] A random-effect model was applied for adjusting the possible heterogeneity arising across the different studies. Heterogeneity was assessed using χ^2 test and I^2 statistics. The statistical analysis was performed using MetaXL, software Version 5.3 (EpiGear International Pty Ltd, Sunrise Beach, QLD, Australia). The study was carried out in accordance with the declaration of Helsinki and within the terms of the local legislation.

The initial electronic search generated a total number of 14 documents after elimination of replicates, 10 of which were immediately excluded because they did not clearly report serum prealbumin values (n = 5), did not stratify serum prealbumin values in COVID-19 patients with different illness severity (n = 3), and the endpoint was not clearly defined (n = 1), while the remaining document ought to be excluded as it could not be found in the journal website. Another eligible study was identified from the reference list, so that our final analysis included five studies,[5-9] all cross-sectional, totaling 1813 COVID-19 patients, 269 (14.8%) with severe disease (Table 1). All studies were carried out in China, while severe COVID-19 illness was defined as a respiratory failure in three studies, and prolonged hospitalization or death in the remaining two investigations.

The outcome of single studies and their pooled analysis are shown in Figure 1. In 4 of 5 (80%) studies, serum prealbumin levels were significantly lower in COVID-19 patients with severe illness, while in the remaining investigation, the concentration did not vary significantly in patients with or without severe disease, defined as prolonged hospitalization (ie, >12 days). In the pooled analysis, the serum prealbumin value in COVID-19 patients with severe illness appeared significantly lower (WMD, −61.80 mg/L; 95% CI, −98.63 to −24.96 mg/L; I^2, 99%) compared with those with milder disease. The elimination of the study of An et al,[5] which used prolonged hospitalization as an endpoint, amplified this difference (WMD, −77.48 mg/L; 95% CI, −118.17 to −36.78 mg/L; I^2, 99%).

The findings of this meta-analysis of available scientific literature attest that serum prealbumin values are significantly lower in

TABLE 1 Summary of clinical studies that investigated prealbumin values in coronavirus disease 2019 (COVID-19) patients with or with severe illness

Study name	Setting	Study design	Sample size	Age	Females	Endpoint
An et al[5]	China	Cross-sectional	47	47 ± 5 vs 39 ± 7	49%	Prolonged hospitalization
Duan et al[6]	China	Cross-sectional	348	58 ± 15 vs 44 ± 15	47%	Respiratory failure
Ji et al[7]	China	Cross-sectional	102	N/A	52%	Respiratory failure
Luo et al[8]	China	Cross-sectional	1115	70 ± 12 vs 59 ± 15	49%	Death
Wu et al[9]	China	Cross-sectional	201	47 ± 4 vs 59 ± 5	36%	Respiratory failure

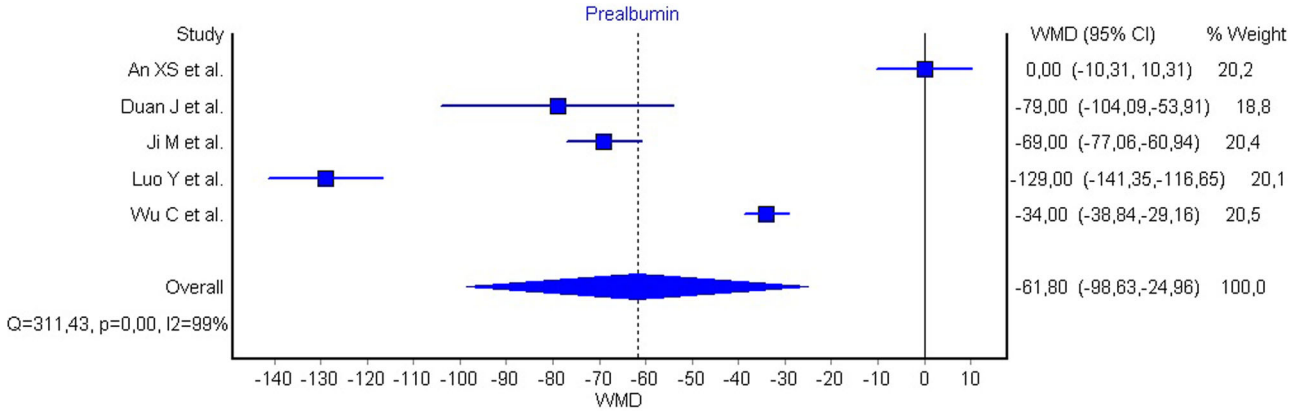

FIGURE 1 Weighted mean difference (WMD) and 95% confidence interval (95% CI) of antithrombin values in coronavirus disease 2019 (COVID-19) patients with severe illness compared with those with milder disease

COVID-19 patients developing more severe illness. It is also important to report here the findings of another study, which was omitted from our analysis as the serum prealbumin values were unavailable in COVID-19 patients with or without severe illness. Briefly, Zuo et al[10] prospectively studied 446 COVID-19 elderly patients, followed-up during their hospital stay. In a fully adjusted model, COVID-19 patients in the lowest tertile of serum prealbumin displayed a nearly threefold higher risk of mechanical ventilation (odds ratio, 2.8; 95% CI, 1.2-6.8), a 25-fold higher risk of intensive care (odds ratio, 26.4; 95% CI, 4.0-172.4) and a 19-fold higher risk of death (odds ratio, 20.1; 95% CI, 3.6-111.6) compared with those in the highest serum prealbumin tertile.

According to this evidence, we can hence conclude that the progressive decline of serum prealbumin values in COVID-19 reflects a deteriorated clinical status, and may also be considered an additional contributing and predictive factor for enhancing the risk of developing unfavorable disease progression, up to death.[8]

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