Correlation of rate of serum albumin decline with other acute phase reactants and effect of current treatment options on serum albumin level in COVID-19

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Dear Editor,

I have read the study "ALLY in fighting COVID-19: magnitude of albumin decline and lymphopenia (ALLY) predict progression to critical disease"[1] with great interest but would like to bring some issues to the notice of the readers.

First, the study used a comorbidity score to calculate the number of comorbidities present at admission out of asthma, coronary artery disease, chronic obstructive pulmonary disease, diabetes mellitus, hypertension, cancer, history of renal disease, and smoking.[1] Liver disease has not been considered in the comorbidity scale, which can greatly influence the albumin level at any given time and the rate of its decline.

Second, systemic inflammation is common in severe COVID-19. Inflammation has been shown to cause the escape of serum albumin into the interstitial space due to increased capillary permeability, and eventually lead to increased volume distribution of albumin.[2] Interleukin 6 (IL-6) contributes to vascular hyperpermeability, leakiness, hypotension, and pulmonary dysfunction.[3] The study could not correlate the magnitude and the rate of albumin change with inflammatory biomarkers such as C-reactive protein (CRP) or IL-6 which were not consistently available over the course of admission.[1] This means that the study could not make a conclusion that the albumin decline of 0.9 g/dL or greater within 5 days of admission was solely due to COVID-19-induced inflammatory state. Correlating the albumin level with CRP and IL-6 would have helped to rule out the effect of comorbidities and confounders which might have affected albumin levels.

Third, the study mentions that the analysis was performed at the time when steroids were discouraged by the WHO guidelines,[1] so considering an albumin drop of 0.9 g/dL or greater within 5 days of admission as a factor for higher risk of disease progression might not be correct at present due to the availability of various treatment options such as corticosteroids and IL-6 inhibitors that suppress cytokine storm.[4] The effect of such drugs on albumin level in patients with COVID-19 needs to be investigated as they might have an effect on the rate of albumin decline.

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