Dynamic albumin values as clinical surrogate for COVID-19 therapeutics

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We are delighted to see a letter to the editor[1] essentially agreeing with the message conveyed through our retrospective observation: that a dynamic, accelerated fall of albumin levels in patients admitted with severe COVID-19 predicts progression to critical COVID-19.[2] Our express intent was to spur further clinical investigation.

Our conclusion remains unchanged after accounting for pre-existing liver disease. COVID-19 frequently causes a self-limited transaminitis in patients without liver disease. Liver function measured at hospital admission using alanine aminotransferase and aspartate aminotransferase for the patients in our study who progressed to critical disease, compared with those who did not progress, was similar (table 2 in ref 2), and the prevalence of hepatic failure during the course of the admission by baseline disease severity was also similar.

We studied patients admitted for management of COVID-19. Thus, dynamic changes clearly reflect COVID-19 disease. We posited that albumin levels fall dynamically due to the hyperinflammatory pathophysiology of COVID-19, with attendant capillary leak.[2] We are delighted that the author of the above letter shares our burning question: does the dynamic fall of serum albumin track the hyperinflammatory markers of C-reactive protein, ferritin, and interleukin 6 (IL-6), and do immunomodulators such as glucocorticoids or anti-IL-6 receptor or anti-IL-6 cytokine monoclonal antibody therapies reverse this? This is an important avenue for future investigation. As IL-6 values are not routinely measured, that question can only be addressed prospectively.

Finally, we direct the letter writer to the discussion section of our published manuscript, where we have expressly addressed the potential that glucocorticoids might attenuate the finding we observed. Steroids,[3] and possibly other immunomodulators, favorably impact clinical outcomes in patients hospitalized with severe COVID-19 pneumonia and hypoxemia, appearing to attenuate the dynamic decline and/or spur recovery of serum albumin levels (unpublished observation). Steroids being standard of care now for these hypoxemic inpatients, prospective randomized analysis would be unfeasible for steroids due to absence of equanimity, yet tractable for assessment with add-on immunomodulation.

The closing of our original manuscript rings true today: 'Finally, we propose that the variables of interest identified in our risk model should be included as risk markers in future treatment studies for COVID-19.'[2]

We hypothesize that interventions of clinical benefit in COVID-19 will attenuate or reverse the dynamic decline in serum albumin levels, and propose that this signal may be a surrogate, early marker for clinical efficacy of therapies for COVID-19.

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