



Hyponatremia: A Marker of Inflammation for COVID-19

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We have read with great interest the article by Nair et al¹ in which they explain the presence of two subphenotypes of acute respiratory distress syndrome (ARDS) secondary to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) through serum markers of systemic inflammation such as ferritin (ferritin), serum lactate dehydrogenase (LDH) and C-reactive protein (CRP), which are associated with worse results in terms of days of stay in the intensive care unit (ICU), days of mechanical ventilation, and higher mortality; interleukin-6 (IL-6) is the proinflammatory cytokine involved in the cascade of systemic damage. Therefore we share our experience and research on the other side of the world: under the premise that elevated serum levels of IL-6² favor non-osmotic secretion of antidiuretic hormone (ADH) with the consequent presence of hyponatremia this electrolyte disturbance could be another marker of severity and poor prognosis; therefore, SARS-CoV-2 would be the etiological agent in which the IL-6 released is recognized as the main inflammatory mediator of the acute phase with hematological, immunological, endocrinological, and metabolic effects.³

Through a retrospective, observational, analytical, single center cohort; held in Veracruz, Mexico in the period from March 18 to June 2, 2021; Patients with a diagnosis of severe pneumonia due to SARS-CoV-2 confirmed with reverse transcriptase polymerase chain reaction (RT-PCR) were recruited. The biochemical variables of systemic inflammation measured on admission to the intensive care unit (ICU) were: lactate dehydrogenase (LDH), C-reactive protein (CRP), ferritin, D-dimer (DD) and serum sodium value finding the following: Ninety-two patients were included of whom

56.5% (52 patients) were nonsurvivors; in this group the values of LDH stand out with a value of 585 mg/dL, CRP 157 mg/dL, ferritin 1119.5 ng/mL, DD 1811.5 ng/mL, serum sodium 135 mg/dL with $p = 0.13, 0.05, 0.35, 0.66, 0.95, 0.05$ consecutively when compared with the group of survivors. On the other hand, when determining them as a risk factor for mortality, only serum sodium less than 135 mg/dL presented statistical significance with an odds ratio (OR) of 4.35 (95% confidence interval [CI]: 1.10–17.09) $p = 0.03$, but not the other variables of systemic inflammation.

In accordance with other investigations, Berni et al⁴ documented that IL-6 levels more than 10 pg/mL in patients with coronavirus disease 2019 (COVID-19) are associated with low plasma sodium (128 mmol/L) with a correlation of -0.6 ($p = 0.006$). In addition, the correlation between low partial pressure of oxygen/fraction of inspired oxygen and hyponatremia was 0.6 ($p = 0.0005$). Hyponatremia was associated with greater severity, that is, mechanical ventilation, ICU admission, and death (53 vs. 7%, $p = 0.031$). On the other hand, plasma sodium levels increased in patients with COVID-19 treated with IL-6 receptor antagonist (tocilizumab). Atila et al,⁵ in their multivariable regression model, documented that doubling IL-6 levels (i.e., 100% increase) decreases plasma sodium -0.97 mmol/L in COVID-19 patients. Likewise, IL-6 more than or equal to 11.0 pg/mL predicts hyponatremia with a 75% area under the curve (sin 58%, esp 86.5%) with OR of 7.4 (95% CI: 3.5–17.4; $p < 0.001$).

This would further support the scientific evidence of two ARDS subphenotypes according to the predominant systemic inflammatory response in the host. Hyponatremia is

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related to a higher level of IL-6 in patients with COVID-19 reflecting hyperinflammation in an accessible and specific way.

Name of the Institution Where the Work was Performed

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Consent for Publication

This was a noninterventional study.

Conflict of Interest

None.

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