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-6 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.

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 = 0006). In addition, the correlation between low partial pressure of oxygen/fraction of inspired oxygen and hyponatremia was 0.6 (p = 00005). 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 an 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
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

Consent for Publication
This was a noninterventional study.

Conflict of Interest
None.

References