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Haematological inflammatory prognostication in COVID-19: Points to ponder!



Dear Editor,

We read with great interest the research reports of haematological inflammatory prognostication in COVID-19 featured recently in the *Journal* [1,2]. While the Seyit et al. elucidation of elevated haematological ratios such as neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) in COVID-19 subset [1] and the Moradi et al. depiction of COVID-19 mortality predictive value of NLR are promising [2], additional points mandate elaboration to render a more comprehensive purview of this parsimonious prognostication.

- (i) The lack of comparative data on the platelet counts in Moradi et al. study merits attention, particularly when a prognostic potential has been attributed to PLR in a COVID-19 setting studied by Qu et al. [3]. This becomes all the more relevant in the light of Fois and colleagues description of an independent COVID-19 mortality predictive value of a combined platelet-leukocytic index or the systemic immune-inflammation index (SII = neutrophil \times platelet-to-lymphocyte ratio) in their retrospective evaluation of 119 COVID-19 patients [4]. Furthermore, SII emerged as the sole COVID-19 prognostic haematological parameter (Hazard ratio: 1.0001; 95% confidence interval: 1.0000 to 1.0001; p value: 0.029) subsequent to a multivariate Cox regression analysis in their evaluation of the mortality predictive potential of indices like SII, systemic inflammation response index (SIRI = neutrophil \times monocyte-to-lymphocyte ratio) and the aggregate index of systemic inflammation (AISI = neutrophil \times platelet \times monocyte-to-lymphocyte ratio) alongside the conventionally described ratios like NLR, PLR and monocyte-to-lymphocyte ratio (MLR) [4].
- (ii) While the Moradi et al. retrospective study classifies the included 219 COVID-19 patients premised on the peripheral oxygen saturation values at admission ($SpO_2 \leq 90\%$ and $>90\%$), it fails to account for the subsequent oxygenation parameters during the course of the disease, particularly with 63 participants requiring intensive care unit (ICU) admission in their study [2]. The importance of the respiratory physiological status assessment is highlighted in the Qu et al. finding of a severe pneumonia in COVID-19 patients with increased PLR [3]. In this context, Fois et al. also describe substantially worse partial pressure of arterial oxygen/fractional inspired oxygen concentration (PaO_2/FiO_2) ratios in COVID-19 patients with an elevated SII [4].
- (iii) As an extension of the same, Fois et al. propose a potential ability of SII to reflect the pulmonary consequences of COVID-19 independent of the comorbidity status supported by the insignificant differences in the respective Charlson comorbidity index (CCI) between the groups with or without SII greater than the cut-off

value of 1835 in their study in background of significantly dismal PaO_2/FiO_2 ratios in the high SII group as discussed above [4]. Herein, the incorporation of a composite comorbidity index like CCI alongside PaO_2/FiO_2 ratios and/or chest computed tomography (CT) severity scores in Moradi et al. study could have assisted the authors in a much required exploration of the intriguing links between the haematological prognostic markers and the pulmonary inflammatory sequel in COVID-19 patients [3–5].

- (iv) Lastly, in addition to the patient-related factors and hospital admission-parameters which mandate adjustment for a NLR outcome predictive assessment in Moradi et al. study, various other overlooked factors over the stipulated disease course like the level of care and the end-organ failure indicators, etc. could have possibly confounded a sound predictive potential evaluation, necessitating a careful interpretation of the results [6,7].

Amidst the ever growing interest in haematological risk prediction across diverse clinical settings predisposed to inflammation [8,9], this initial retrospective literature also endorses a strong case for haematological inflammatory prognostication in COVID-19. Nevertheless, pragmatic prospective evaluation should closely back up the initial encouraging results in order to assist in an early, parsimonious and comprehensive risk-stratification of COVID-19 cohort which could further enable the optimal implementation of risk-based individualised management.

Credit authorship contribution statement

Rohan Magoon: Writing - original draft. **Ankur Jain:** Conceptualization, Writing - review & editing.

Declaration of Competing Interest

We do not have any conflict of interest, any commercial or financial interest in this material & agree to abide by the rules of your journal regarding publication of this article.

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