

shown significant responses to therapeutics that mechanistically target cytokine signaling pathways (1). Whereas cytokine-directed therapies in patients with systemic bacteremia and sepsis have failed to demonstrate any clinical benefit (2). Consequently, measuring serum cytokines for certain conditions, such as rheumatoid arthritis, may potentially underrepresent, or perhaps even misrepresent, the true impact of cytokine release during the associated inflammatory state at the tissue level.

Similar to the range of toxicity seen with various endotoxins, as discussed by Honore et al., the downstream impact of various cytokines on inflammation is variable and often not correlated with each other as outlined in our manuscript (3). It is for this reason that we argue that the term “cytokine storm” is misrepresentative of the complex inflammatory response encountered in various diseases and conditions.

Allan E. Stolarski
Jiyoun Kim
Qiuyang Zhang
Daniel G. Remick
Department of Surgery
and Department of Pathology
Boston University, Boston Medical Center
Boston, Massachusetts
Allan.Stolarski@bmc.org

The authors report no conflicts of interest.

REFERENCES

1. McInnes IB, Schett G: Pathogenetic insights from the treatment of rheumatoid arthritis. *Lancet* 389:2328–2337, 2017.
2. Remick DG: Cytokine therapeutics for the treatment of sepsis: why has nothing worked? *Curr Pharm Des* 9:75–82, 2003.
3. Stolarski AE, Kim J, Zhang Q, Remick DG: Cytokine drizzle—The rationale for abandoning “Cytokine Storm.” *Shock* 56(5):667–672, 2021.

Neutrophil-to-Lymphocyte Ratio and Covid-19

To the Editor: We read with great interest the article recently published by Tatum et al. (1) entitled “Neutrophil-to-lymphocyte ratio and outcomes in Louisiana COVID-19 patients.” They found that neutrophil-to-lymphocyte ratio (NLR) is a prognostic factor for endotracheal intubation on hospitalization and an independent predictor of mortality risk in SARS-CoV-2

patients. We thank the authors for their valuable contribution to the literature in these difficult conditions. However, we think there are some points that need to be discussed.

The drug use of the patients has not been mentioned in this article and it would be appropriate to mention the use of drugs such as glucocorticoids that may affect the NLR value. As it is known, while the neutrophil count increases with the use of glucocorticoids, other circulating cells such as eosinophils, monocytes, and lymphocytes are reduced (2). This is an indication that it affects NLR values, and it would be more appropriate for the authors to report how many patients were taking corticosteroids.

NLR, one of the routine blood parameters, has been extensively studied in many diseases and remains important (3). Studies have reported that NLR is significantly higher in applications related to infection. Similarly, stress factors such as trauma and gastrointestinal system bleeding may cause increases in NLR (4, 5). Therefore, providing useful information about infection, malignancy, alcohol use, smoking, gastrointestinal bleeding, renal/metabolic conditions, encephalopathy, surgical procedures, and additional medical procedures that may affect NLR values will provide useful information. As a result, NLR can be affected by many factors. The prognostic routine clinical use of these parameters in COVID-19 patients is not yet reasonable. Prospective and multicenter studies are needed.

Cihan Bedel
Mustafa Korkut
Department of Emergency Medicine Health Science University
Antalya Training And Research Hospital Antalya, Turkey
cihanbedel@hotmail.com

The authors report no conflicts of interest.

REFERENCES

1. Tatum D, Taghavi S, Houghton A, Stover J, Toraih E, Duchesne J: Neutrophil-to-lymphocyte ratio and outcomes in Louisiana COVID-19 patients. *Shock* 54(5):652–658, 2020.
2. Frenkel A, Kachko E, Cohen K, Novack V, Maimon N: Estimations of a degree of steroid induced leukocytosis in patients with acute infections. *Am J Emerg Med* 36(5):749–753, 2018.
3. Bedel C, Selvi F: Association of platelet to lymphocyte and neutrophil to lymphocyte ratios with in-hospital mortality in patients with type A acute aortic dissection. *Braz J Cardiovasc Surg* 34(6):694–698, 2020.
4. Liu S, Liu X, Chen S, Xiao Y, Zhuang W: Neutrophil-lymphocyte ratio predicts the outcome of intracerebral hemorrhage: a meta-analysis. *Medicine (Baltimore)* 98(26):e16211, 2019.
5. Manoochehry S, Vafabin M, Bitaraf S, Amiri A: A comparison between the ability of revised trauma score and Kampala trauma score in predicting mortality: a meta-analysis. *Arch Acad Emerg Med* 7(1):e6, 2019.