https://doi.org/10.46389/rjd-2022-1170
www.rjdnmd.org

Rom J Diabetes Nutr Metab Dis
2022; volume 29, issue 3, pages 374-375

Letter to the Editor

Association of the blood neutrophil-to-lymphocyte ratio with the pathogenesis of COVID-19-related thyroid conditions

Zohreh Jadali[1]*

[1] Department of Immunology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

* Correspondence to: Zohreh Jadali, Department of Immunology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran. Phone: 6462268-6465404; Fax: (+98 21) 6462267; E-mail: zjadali@razi.tums.ac.ir/zjadali@yahoo.co.uk

Received: 1 May 2022 / Accepted: 27 July 2022

Dear Editor,

Severe acute respiratory syndrome coronavirus 2(SARS-CoV-2) can adversely affect different organ systems like the thyroid. The immune system plays a pivotal role in the control and progression of COVID-19. Therefore, the evaluation of the immune responses in infected patients with a routine laboratory test is one of the most effective ways to keep track of disease. The neutrophil-to-lymphocyte ratio(NLR) is a marker for evaluating the systemic inflammatory response. High NLR could be observed in inflammatory conditions caused by different factors, including infections. The current understanding of SARS-CoV-2 pathogenesis suggests a central role in exaggerated inflammatory responses.

Therefore, analysis of NLR changes could reflect the change in inflammatory reactions. To date, different studies have evaluated the role of NLR in COVID-19 patients. Many, but not all studies have suggested that NLR is correlated with the presence of COVID-19 and its activity. For instance, Tan *et al.* demonstrated an inverse correlation between lymphocyte percentage with disease severity and prognosis [1]. These findings are consistent with other studies, which showed that severe cases of COVID-19 tended to have higher neutrophil counts and lower lymphocyte levels [2].

Current literature also indicates that changes in NLR may be a reliable prognostic marker for different thyroid disorders, including Hashimoto's thyroiditis [3]. Therefore, COVID-19 patients with thyroid dysfunction are more likely to have increased NLR levels. Unfortunately, there is limited experience regarding the clinical value of NLR in COVID-19 patients with thyroid abnormalities. In one study, Sciacchitano *et al.* indicated an association between increased NLR and low FT3 serum levels in infected patients. They also identified a significant correlation between the low FT3 values and clinical and radiologic disease severity scores [4]. Yazan *et al.* also demonstrated a significant relationship between neutrophil count, C-reactive protein (CRP), TSH, FT3, and FT4 with ICU admission. In this study, 108 diseased individuals had euthyroid sick syndrome (ESS) and were classified as mild and moderate.

Interestingly, neutrophil count in moderate ESS cases was higher than in those with euthyroid and mild ESS [5]. Similarly, Zhang *et al.* indicated that neutrophil counts and inflammatory marker levels, including CRP, were significantly elevated in COVID-19 patients with thyroid dysfunction [6]. Evidence also suggests a possible link between lymphopenia and abnormal thyroid function in patients with severe COVID-19. A recent study indicates a significant decrease in TSH, T4, FT4, and T3 plasma concentrations in severe lymphopenic COVID-19 patients compared to patients without lymphopenia [7]. The exact molecular mechanisms of NLR changes in COVID-19 patients with thyroid dysfunction are obscure. A high neutrophil percentage may be due to persistent infection and prolonged hypoxia. This can lead to bone marrow hyperplasia and an increase in circulating neutrophils.

Moreover, neutrophil longevity increases under inflammatory conditions. This can help the development of inflammation and inflammation-associated co-morbidities [8]. A reciprocal relationship between the thyroid hormones and neutrophils may also play a role in neutrophil count and function changes. Thyroid hormones can regulate neutrophil activities which are

reflected by the increased number of neutrophils and enhanced respiratory burst after stimulation with thyroid hormone. Lymphocytopenia in COVID-19 patients with thyroid dysfunction has been suggested to result from lymphocyte recruitment to the respiratory tract, adhesion to inflamed respiratory vascular endothelium, the induction of lymphocyte apoptosis by virus or increased splenic clearance of infected lymphocytes. The impaired abilities of T cells may also be attributable to altered T cell activation and differentiation, which sequentially affects the function and phenotypic plasticity of CD4+ T cell subsets [9].

Additionally, thyroid hormones are responsible for homeostatic regulation and the function of lymphocyte populations. Therefore, lymphopenia may be linked with abnormal thyroid function in severe cases of COVID-19. This idea is supported by a recent study that reported significantly decreased plasma concentrations of TSH, T4, FT4, and T3 in severe lymphopenic COVID-19 patients compared to patients without lymphopenia [7]. Overall, NLR may serve as a predictor marker in COVID-19 patients with thyroid disorders. However, further studies are needed to identify the exact mechanisms.

Conflict of interest

The author declares no conflict of interest.

References

1. Tan L, Wang Q, Zhang D *et al.* (2020). Lymphopenia predicts disease severity of COVID-19: a descriptive and predictive study. Signal Transduct Target Ther. 5(1):33.
2. Feng X, Li S, Sun Q *et al.*(2020). Immune-inflammatory parameters in COVID-19 cases: A Systematic Review and Meta-Analysis. Front Med (Lausanne). 7:301.
3. Bilge M, Yesilova A, Adas M *et al.* (2019). Neutrophil- and platelet- to lymphocyte ratio in patients with euthyroid hashimoto's thyroiditis. Exp Clin Endocrinol Diabetes. 127(8):545-549.
4. Sciacchitano S, De Vitis C, D'Ascanio M *et al.* (2021). Gene signature and immune cell profling by high-dimensional, single-cell analysis in COVID-19 patients, presenting Low T3 syndrome and coexistent hematological malignancies. J Transl Med. 19(1):139.
5. Yazan CD, Ilgin C, Elbasan O *et al.*(2021). The association of thyroid hormone changes with inflammatory status and prognosis in COVID-19. Int J Endocrinol. 2021:2395212.
6. Zhang Y, Lin F, Tu W *et al.* (2021). Thyroid dysfunction may be associated with poor outcomes in patients with COVID-19. Mol Cell Endocrinol. 521:111097.
7. Grondman I, Nooijer AH de., Antonakos N *et al.*(2021). The association of TSH and thyroid hormones with lymphopenia in bacterial sepsis and COVID-19. J Clin Endocrinol Metab. 106(7):1994-2009.
8. Galani IE, Andreakos E.(2015). Neutrophils in viral infections: Current concepts and caveats. J Leukoc Biol98(4):557-564.
9. Chen Z, Wherry EJ. (2020). T cell responses in patients with COVID-19. Nat Rev Immunol. 20(9):529-536.