

## Letter to the Editor

## Editöre Mektup

***HIF-1 $\alpha$  pathway is associated with neutrophil-to-lymphocyte ratio in patients with renal artery stenosis***

To the Editor,

We read the article “Hematological indices in renovascular hypertension: A propensity score matching analysis” by Gurbuz et al.<sup>[1]</sup> with great interest. The authors found that a strong indicator of inflammation, the neutrophil-to-lymphocyte ratio (NLR), was significantly higher in patients with renal artery stenosis when compared to patients with essential hypertension. This finding was linked to an increased inflammatory state due to renal artery stenosis.

Hypoxia-inducible factor (HIF) is a key transcription factor that facilitates cellular adaptation to hypoxia, and consists of  $\alpha$  and  $\beta$  subunits. The  $\alpha$  subunit of HIF is regulated by oxygen and its expression is induced by hypoxia. HIF-1 $\alpha$  plays a significant role in the survival of neutrophils via the nuclear factor- $\kappa$ B pathway, which is important for neutrophil apoptosis.<sup>[2]</sup> Elks et al.<sup>[3]</sup> also demonstrated in a zebrafish model that HIF-1 $\alpha$  delays the resolution of inflammation by inhibiting both neutrophil apoptosis and neutrophil migration to the inflammation site.

Renal artery stenosis causes renal ischemia and activates the renin-angiotensin-aldosterone pathway. HIF-1 $\alpha$  levels increase due to renal ischemia.<sup>[4]</sup> As mentioned above, HIF-1 $\alpha$  has effects on neutrophil counts and inflammation through several mechanisms.

To conclude, an increased NLR in patients with renal artery stenosis should not be solely linked to inflammation. Although a high inflammatory state due to an activated renin-angiotensin-aldosterone system may be responsible for a high NLR in patients with renal artery stenosis, HIF-1 $\alpha$ -related inhibition of neutrophil apoptosis may be another important mechanism that should not be forgotten.

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