Commentary: Systemic immune-inflammatory indices and their association with ocular disorders—Do we have economical and reliable biomarkers?

Recent advances suggest that inflammation is not just a local response but can be considered a systemic process. Blood levels of monocytes, neutrophils, and lymphocytes are invariably altered in systemic inflammation.[1] Therefore, certain immune-inflammatory indices are currently being investigated as markers of systemic inflammation in cardiovascular disorders, connective tissue disorders, infections, diabetes mellitus, and cancers.[1]

In inflammation, hematologic evaluation shows neutrophilia and relative lymphocytopenia. This is reflected as an increase in neutrophil-lymphocyte ratio (NLR).[2] In inflammation, it is understood that monocytes are a major source of proinflammatory mediators.[3] On the other hand, high-density lipoprotein (HDL) contributes to neutralization of these proinflammatory effects by various mechanisms. Lowering endothelial vascular cell adhesion molecule 1 (VCAM 1) expression, increased production of nitric oxide synthase, and inhibition of monocyte migration are the modes by which HDL contributes to systemic anti-inflammatory processes.[4] An increase in the monocyte-HDL ratio (MHR), is therefore suggestive of a dominant proinflammatory state. These ratios are more powerful predictors of inflammation than individual values as they combine the predictive importance of two different variables into a single unit.

In ophthalmology, NLR and MHR have been assessed in patients with dry-eye disease, keratoconus, pseudoexfoliation, glaucoma, ischemic optic neuropathies, and retinal vein occlusions.[5] In diseases that have been investigated, where an immune or inflammatory component is part of the pathogenic mechanisms, these indices appear to be reliable biomarkers. Since there are no molecules that are uniformly accepted as biomarkers for ocular disorders, research into identifying such a biomarker is the need of the hour. Investigations that can help to elucidate the mechanisms involved or provide information to the treating clinician on the possible future course of the disease is definitely a welcome addition to our armamentarium. In this regard, systemic immune-inflammatory markers serve an important purpose as they are readily available to all clinicians and are cost-effective.

Central serous chorioretinopathy (CSCR), that is characterized by spontaneous detachment of the retina with or without simultaneous retinal pigment epithelial (RPE) detachments, is primarily attributed to increased permeability of choroidal vessels along with some degree of impairment in RPE function.[6] However, as a disease, its pathogenesis is not fully understood. Multifactorial pathways and complex

systemic associations are implicated.[7] Research has established the role of catecholamines and cortisol in the disease process. Few other systemic factors are related to CSCR. Among them, genetic predisposition with polymorphisms in complement factor H and Cadherin gene, psychological stress and type A personality traits are important. Although there is no direct evidence to suggest that systemic inflammation is involved in its pathogenesis, elevated endogenous cortisol and reduced antioxidant capacity in these patients suggest that there could be a role.[8] A low-grade intraocular inflammatory state in eyes with chronic CSCR has also been described.[9] Systemic therapy has been tried and they target these etiologic pathways.[7] In their research, Sirakaya *et al*. have used this inflammatory hypothesis to test the association of systemic indices with acute CSCR.[10]

In CSCR, Erol and colleagues have demonstrated that NLR and C-reactive protein (CRP) are higher in patients with acute CSCR when compared to normal volunteers and patients with chronic CSCR.[11] They also noted that, in chronic CSCR, mean platelet volume was higher. The present paper by Sirakaya *et al*. attempts to shed more light in this domain by assessing MHR along with NLR, CRP, and erythrocyte sedimentation rate (ESR). Although the present paper differs from the former in reporting that NLR and CRP along with ESR were not elevated in patients with acute CSCR, they report that increased MHR appears to be associated with CSCR. Based on their results, they suggest that systemic inflammatory processes contribute to CSCR. Of particular note, the former has studied both acute and chronic CSCR while the latter have included only acute CSCR patients in their study. The association of these systemic indices with both acute and chronic CSCR merits attention as further research has the potential to identify patients who might progress from acute to chronic variety that is associated with increased visual morbidity.

Such immune-inflammatory markers are not infallible. They can be influenced by other acute systemic states such as stress, fever, infections, systemic therapy for the concomitant disease, dehydration, and lifestyle factors such as diet and exercise. Therefore, when using these markers as scales to assess the severity of ocular pathologies, due diligence has to be given to eliminating these fallacies.

Presently available literature does show promise in identifying economical, widely available and reliable biomarkers. They can be investigated for other ocular diseases such as diabetic macular edema and uveitis. Besides providing evidence of the association of systemic inflammation with ocular diseases, analyzing the natural course of the disease in relation to these indices is also possible. Although evidence is encouraging, we await prospective studies in different ethnic groups involving more participants before we can use these in our daily practice.

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