

## Paradoxical relationship between inflammation-related molecules and postoperative complications after general anaesthesia

Dear Editor,

I read the article by Tharavath *et al.*<sup>[1]</sup> about the association between high C-reactive protein (CRP)-albumin ratio (CAR) as an informative marker of inflammation and a higher need for mechanical ventilation in patients who have had an operation under general anaesthesia. These findings are important because perioperative inflammation is associated with different complications. Therefore, assessing highly sensitive inflammatory markers such as CRP and albumin and identifying their

molecular mechanisms are paramount for improving perioperative outcomes. It is important to understand these molecules' physiological and pathophysiological role during inflammatory conditions as these have different pro- and anti-inflammatory activities.

CRP belongs to the pentraxin family of proteins and occurs in at least two different conformational forms: pentameric CRP (pCRP) and monomeric CRP (mCRP). The conformational conversion of pCRP to mCRP has been revealed to play a critical role in the action of CRP.<sup>[2]</sup> After binding to a specific ligand, pCRP, which is particularly abundant in plasma, exhibits anti-inflammatory properties. These have been shown to occur through multiple mechanisms, including increasing interleukin (IL)-1 receptor antagonist expression in human peripheral blood mononuclear cells, increasing anti-inflammatory cytokines, and down-regulation of pro-inflammatory cytokines. Upon stimulation at inflammatory sites, pCRP undergoes

a structural change and is converted into mCRP. mCRP, which is preferentially expressed in tissues and has a decreased aqueous solubility, exerts strong pro-inflammatory activity via different mechanisms including activation of the complement cascade, development of pro-inflammatory macrophages, platelet activation and thrombus growth, and increasing the production of inflammatory cytokines.<sup>[3]</sup> Because of the distinctive bioactivities of pCRP and mCRP, it seems necessary to clarify the functional impact of CRP isoforms in inflammatory processes. This issue is important because many previous studies have not been clear on which CRP isoform was measured.

Another inflammatory mediator measured by this study is albumin.<sup>[1]</sup> The authors found that patients who required postoperative mechanical ventilation showed a significant reduction in serum albumin concentration. The potential link between surgical adverse outcomes and hypoalbuminemia has been found for many years.<sup>[4]</sup> Low albumin levels due to inflammation and surgical trauma may contribute to delayed wound healing, surgical site infections, prolonged hospitalisation, and even death. Hypoalbuminemia may decrease its antioxidant, immunomodulatory, oncotic, and endothelial stabilising activities. Nonetheless, several points should be considered to avoid misinterpretation of the findings. For instance, the estimation of serum albumin is usually performed at a single point in time. At the same time, calculating protein abundances in diagnosing human disease requires a repeated measure. This issue should not be underestimated because CRP and albumin may vary at different phases of the inflammatory process. The concept of 'effective albumin concentration' refers to the content of albumin that is structurally and functionally intact. Modification of serum albumin structure could change its physicochemical properties. For instance, in its native form, albumin has multiple anti-inflammatory activities. However, some post-translational modification of albumin due to a pro-inflammatory micro-environment could alter the properties of the native form, which in turn can alter its anti-inflammatory activities and impair its antioxidant functions.<sup>[5]</sup>

#### Financial support and sponsorship

Nil.

#### Conflicts of interest

There are no conflicts of interest.

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Submitted: 13-Mar-2024

Accepted: 12-May-2024

Published: 02-Jul-2024

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	DOI: 10.4103/ija.ija_278_24

**How to cite this article:** Jadali Z. Paradoxical relationship between inflammation-related molecules and postoperative complications after general anaesthesia. *Indian J Anaesth* 2024;68:736-7.

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