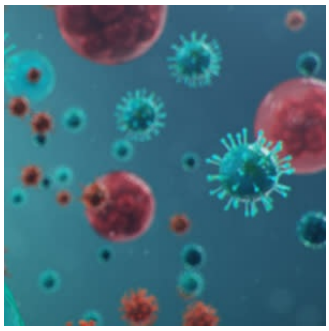
ICU
MANAGEMENT & PRACTICE

What is the Relevance of Cytokine Storm to COVID-19?



COVID-19, in its most severe form, leads to life-threatening pneumonia and acute respiratory distress syndrome (ARDS). In patients with this severity of the coronavirus, mortality rate can approach 40 to 50%.

The mechanism of COVID-19 induced lung injury is still vague, but the term cytokine storm is being used quite frequently in scientific publications as well as the media. What is this cytokine storm and what is its relevance to COVID-19?

As such, there is no definition of a cytokine storm. It basically refers to a hyperactive immune response characterised by the release of interferons, interleukins, tumour necrosis factors, chemokines, and other mediators that are a part of an innate immune response essential for the efficient clearance of infectious agents. Hence, the term cytokine storm implies that the levels of released cytokines have reached a point where they become injurious to host cells.

The problem is that the interaction of these mediators and the pathways that they inform are neither linear nor uniform. Most of the mediators that are implicated in this storm demonstrate pleotropic downstream effects. They are also interdependent in their biological activity. Even if their levels are high, they do not imply pathogenesis. The entire process is quite complex.

Nevertheless, cytokine storm has been associated with COVID-19. Early cases of COVID reported levels of plasma cytokines that were much higher than the normal range, but they were lower than plasma levels in previous cohorts of patients with ARDS. IL-6 median values are above the normal range in many cases well but are lower than the median values that are reported in ARDS. Median values in trials conducted by the National Heart, Lung and Blood Institute's ARDS Network are almost 10 to 40-fold higher. However, it is important to keep in mind that the hyperinflammatory phenotype of ARDS is characterised by elevated pro-inflammatory cytokines; hence this is consistent with the cytokine storm. Median IL-6 levels in patients with a hyperinflammatory phenotype of ARDS are nearly 10 to 200-fold higher compared to levels in patients with severe COVID-19.

The association of COVID-19 and cytokine storm has resulted in the use of immunomodulatory therapies such as IL-6 inhibitors and high-dose corticosteroids. Other monoclonal antibody drugs are also being proposed for treating patients with chronic inflammatory conditions. While these therapies may be effective in COVID-19, is it possible that clinicians would see more success if they selected the right patients for this intervention?

We already know that dexamethasone has also shown positive results in patients with COVID-19 and ARDS. Doesn't that suggest that it may be a good idea to study local inflammatory responses to COVID-19 in the lungs?

It is entirely possible that the term cytokine storm may be misleading in COVID-19 ARDS. The elevated mediators in the so-called storm may be due to endothelial dysfunction and inflammation leading to fever, tachycardia, tachypnoea and hypotension. The term cytokine storm is being thrown around left, right, and centre, but we still need more substantial data to support the theory that cytokine storm is linked to COVID-19.

Source: JAMA

Image Credit: iStock

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