

Immunological Reactions in Severe COVID-19 Requiring Intensive Care Unit Admission

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Previous studies demonstrated an increased severity towards the closely related SARS-CoV diseases in persons with HLA-B*46:01 [1]. Differences in HLA haplotype may influence the persons' response to SARS-CoV-2 (COVID-19) infection and some haplotypes may be associated with increased disease severity. Thus, HLA genotyping may help in identifying persons at risk. COVID-19 testing along with HLA genotyping is highly recommended to predict susceptibility to disease severity and assisting in future vaccination strategy plan.

In acute respiratory distress syndrome (ARDS), IL-1 β and its family (IL-18, IL-33) are significant players to increase the recruitment of immune cells subsequent production of cytokines [2]. IL-1 β and TNF- α are required to develop Th17 cells and assist in Th17 mediate immune response and increased vascular permeability [2]. IL-17 and GM-CSF, cytokines of the Th17 pathway increasing in patients with severe COVID-19 [3] have researchers urgently investigate the role of Th17 in severe COVID-19 cases [4]. Th17 cell-increased expression in the peripheral blood of patients with COVID-19 indicates a player in the COVID-19 cytokine storm as reported in the patients with MERS and SARS [5]. Some Th17 pathway-specific cytokines, such as GM-CSF, IL-1 β , IL-17 and TNF- α are elevated in severe COVID-19 patients [3]. A case study on severe COVID-19 demonstrated an elevated count of Th17 cells, activated CD4+, and CD8+ T cells [6], whereas another previous study revealed a decrease in Th17 subset indicated by low IL-17 secretion urges the need to investigate the role of Th17 specific response in COVID-19 [7]. An increased IFN- γ , IL-1 β , IP-10 and MCP-1 serum concentrations contribute to the activation of Th1 cell response and further aggravation of the cytokine storm like the occurrence in MERS-CoV and SARS-CoV [8,9].

IL-6, a multifunctional cytokine involving the formation of follicular helper T cells, generation of plasma cells, and differentiation of Th 17 cell subsets plays a primary role in cytokine storm that occurs in patients with COVID-19 [10]. IL-6 also inhibit IFN- α , therefore, suppress CD8+ cytotoxic T cells [10]. As demonstrated by PD-1 and Tim-3 expressions, IL-6 induces T cell exhaustion, thus, T cell-mediated immune response might be suppressed during cytokine storm [11]. Role of IL-6 in COVID-19 disease severity has been demonstrated by increased IL-6 levels and its positive association with disease severity [11-18]. A recent report from Germany revealed that COVID-19 cases with IL-6 levels of at least 80 pg/ml had a 22-fold increased risk of respiratory failure with median time to mechanical ventilation of 1.5 days [19] and higher serum IL-6 levels were also reported even 24 hours before death [20,21]. Thus, IL-6 could be used for early detection of COVID-19 patients at risk for respiratory failure as a single parameter or in association with other parameters.

In conclusion, only a small proportion of COVID-19-infected patients progress to severe COVID-19 requiring critical care. In the absence of proper cure of COVID-19, it is necessary to identify the factors that may assist in assessment of the COVID-19 disease severity before rapid progression of the disease.

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