

PATHOPHYSIOLOGIC AND PROGNOSTIC ROLE OF PROINFLAMMATORY AND REGULATORY CYTOKINES IN DENGUE FEVER

Antibody response against Dengue virus – infection with dengue virus induces the production of both neutralizing and non neutralizing antibodies. The neutralizing antibodies are protective in nature. Such antibodies are produced against the infective serotype as well as against other serotype. Hence, protection to infective serotype stays lifelong but cross protection to other serotypes diminishes over few months. The non neutralizing antibodies last lifelong and are heterotypic in nature ie. They are produced against other serotypes but not against the infective serotype. Such antibodies produced following the first serotype infection can bind to a second serotype, but instead of neutralizing the second serotype, it protects it from host immune system by inhibiting the bystander B cell activation antigen against the second serotype. The above phenomenon is called Antibody Dependent Enhancement which explains the reason behind the severity of secondary dengue infection. Being suboptimal in specificity and function, they fail to control infection and, instead, contribute greatly to a ‘cytokine storm’. In addition to the extrinsic ADE pathway, in which the Fc receptor directly facilitates DENV binding onto the cell surface for DENV infection/replication, an intrinsic ADE pathway induces IL-10-mediated immunosuppression. For the intrinsic pathway, the ADE of DENV infection triggers IL-10 production through an immune complex associated with the Fc receptor to enhance the infection severity. In the presence of ADE, the Fc receptor can facilitate viral entry and trigger intracellular signaling. The generation of autoimmunity and ADE may cause concerns for vaccine development against DENV infection. Both viral particles acting through the extrinsic pathway and Fc receptor signaling through the intrinsic pathway are important for IL-10 induction. TNF alpha levels are increased only in those Severe dengue patients who show marked plasma leakage and not in the ones who do not present with symptoms due to thrombocytopenia which explains why negative correlation when compared alone with clinical features and a significant correlation on cumulative comparison. Previous virological and clinical studies showed contribution of high virus replication and low viral clearance from the patient’s body leading to disease severity during DENV infection. In the last few years, several attempts have been made to identify interferon gamma as a serum marker, an adaptive immune cytokine to predict severe dengue. As increased IFN-gamma has been related to diminished viral clearance from the host, disease severity might also be related to its serum level.

Key words : ADE(Antibody Dependent Enhancement), Dengue with warning signs, Cytokine storm