## Secondary Dengue Infection Elicits Earlier Elevations in IL-6 and IL-10 Levels. Clinical and Immunological Insights into disease progression in Posadas, Misiones, Argentina.

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September 13, 2023

## Abstract

Introduction: Dengue virus (DENV) represents a global health concern. Symptomatic infection causes a wide range of clinical manifestations, from mild dengue fever to severe disease, characterized by vascular permeability and bleeding. Previous reports indicated that the exacerbated expression of some cytokines is implicated in the progression of the disease. The aim of this study was to assess IL-6 and IL-10 level kinetics together with the description of clinical parameters, distinguishing two phases within the febrile stage in DENV infected patients. Methods: We conducted a retrospective study on samples from 2016 and 2020 DENV outbreaks in Argentina. Viremic patients were categorized in Phase I and II, based on anti-DENV IgM presence. Cytokine levels, clinical parameters, and type of infection were analyzed. Results: Our analysis included samples from 259 patients in the febrile stage. Of these, 184 patients (71%) were classified into Phase I, while 75 patients (29%) were in Phase II. Ninety-nine patients showed secondary infection (38.2%). Notably, secondary infections exhibited earlier IL-6 and IL-10 elevation than primary infections, suggesting pre-existing immune memory priming the immune response. Thrombocytopenia and elevated AST were associated with Phase II, secondary infection, and hospitalization, and elevated IL-6 and IL-10 correlated with low platelet counts, suggesting their potential as early severity markers. Conclusion: Our findings underscore the pivotal roles played by IL-6 and IL-10 in dengue pathogenesis, with their dynamics varying by type of infection and specific phase within the febrile stage. Further research with broader cytokine panels is warranted to validate these findings.

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