

**Role of natural killer T cells in the pathogenesis of dengue infections**

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**Objectives:** The dengue virus exploits cellular lipid metabolism pathways and natural killer T cells (iNKT), which recognize glycolipids have been suggested to play a role in mouse models of acute dengue. Therefore, we set out to determine if iNKT cells play a role in acute dengue infection

**Methods:** The frequency of iNKT cells (CD3+, V $\alpha$ 24+) was determined in 49 acute dengue and 22 healthy individuals. The functionality and phenotype of iNKT cell subsets were defined only in 19 patients and 10 controls by flow cytometry. Clinical disease severity was determined by the WHO 2011 guidelines

**Results:** The proportion of iNKTs in patients with acute dengue were significantly higher (P=0.03) compared to healthy individuals. We found that the CD4+ iNKTs, which produce inflammatory cytokines and are less cytotoxic, were significantly expanded (p=0.01) in acute dengue. iNKTs of patients were also significantly (p=0.02) more activated (both CD38+ and HLA-DR+), that iNKT cell activation significantly and positively correlated with dengue-specific IgG antibody titres (Spearman's  $r=0.5018$ , P=0.03). iNKT of patients were also predominantly of the immature phenotype, as the expression of CD161 was significantly more than in healthy individuals (p=0.01).

**Conclusions:** As the iNKT cell population, especially of the CD4+ T cell subset appears to be highly activated and expanded in acute dengue, iNKT cells could be contributing to the pathogenesis of dengue infection.