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Expansion of regulatory T cells in acute dengue infection does not associate with disease severity

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Background: Regulatory T cells (Tregs) with suppressive function were shown to expand in acute dengue and were speculated to contribute to milder disease. However, as more recent data point towards a protective role of dengue virus (DENV) specific T cells in acute dengue, we proceeded to determine if the expansion of Tregs in acute dengue was associated with milder clinical disease.

Methods & Materials: 58 adult patients with acute dengue infection were recruited and disease severity classified according to 2011 WHO guidelines. Convalescent samples were obtained from 10 of these patients 30 days after onset of illness. Tregs were identified in both patients and in 13 healthy individuals by staining for CD4+T cells expressing Foxp3 and CD25. Quantitative ELISA was done to determine plasma levels of IL-10, TGFβ and IL-17. Intracellular cytokine staining for IL-17 was carried out and TH17 subset of CD4+T cells was identified as those expressing IL-17 and CD161.

Results: Tregs were significantly expanded in patients with acute dengue ($p < 0.0001$) when compared to healthy individuals and the frequency of Tregs significantly reduced during convalescence ($p = 0.01$). The frequency of Tregs were not significantly higher in those with milder forms of dengue and did not associate with the extent of fluid leakage, presence of shock or liver derangements. The frequency of Tregs in acute dengue, did not correlate with either plasma levels of IL-10 or TGFβ. Expression of CD25, which is the IL-2 receptor, on CD4+T cells was significantly lower ($p = 0.006$) in patients with acute dengue and CD25 expression inversely correlated with IL-10 and TGFβ levels. Both plasma IL-10 ($p < 0.0001$) and TGFβ levels ($p < 0.0001$) were significantly elevated. However, no difference in plasma IL17 levels were observed and the frequency of TH17 subset of CD4+T cells and Treg: TH17 ratios were similar in both patients and healthy individuals.

Conclusion: Although Tregs are increased in frequency during acute dengue, they do not appear to associate with milder clinical disease. Immunosuppressive cytokines (IL-10 and TGFβ) were significantly elevated in patients with acute dengue and inversely correlated with CD25, which suggests that they possibly suppress T cell proliferation.

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Obesity and the presence of asthma are associated with hospitalization due to dengue infection

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Background: Although dengue infections can lead to severe clinical disease sometimes resulting in fatalities, the majority of both primary and secondary dengue infections result in mild/asymptomatic disease that is usually not diagnosed as dengue. Therefore, we proceeded to investigate epidemiological and comorbid risk factors associated with hospitalization when infected with dengue.

Methods & Materials: 1689 healthy individuals who were attending the primary health care facility of the university were recruited. Information regarding their co-morbid illnesses and anthropometric measurements were recorded. The dengue antibody status was determined in all individuals.

Results: Although 1152/1689 (68.2%) individuals were seropositive for dengue and only 133/1152 (11.5%) of them had been hospitalized due to dengue. We found that obesity (BMI > 22.9 in adults and above the 85th percentile BMI for age for children), asthma, allergic rhinitis and a waist circumference of > 80cm in women was significantly associated with increased risk of hospitalization. The association of hospitalization due to dengue and obesity was stronger for females ($P < 0.0001$, odds ratio = 3.33, 95% CI = 1.8 to 6.1), when compared to males (p value = 0.04, odds ratio = 2.2, 95% CI = 1.1 to 4.5). Although female children were significantly more likely ($p = 0.006$) to be hospitalized due to dengue (odds ratio 2.4, 95% CI = 1.3 to 4.4) when compared to male children, no such association was observed in adults. The presence of diabetes, hypercholesterolaemia or hypertension were not significantly associated with hospitalization due to dengue.

Conclusion: Obesity, a high waist circumference in women, asthma and allergic rhinitis appear to be associated with a higher risk of hospitalization when infected with the dengue virus.

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