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**LOWER T CELL APOPTOSIS IN THE SECOND INFECTION WITH HETERO-SEROTYPE DENV**

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The available evidence suggests that dengue virus-specific T lymphocytes and cytokine storm play a pivotal role in the immunopathogenesis of plasma leakage. Investigations are underway to identify the immune profiles associated with increased or decreased risk for severe disease. In this study, CD14+ cells from the peripheral blood mononuclear cells (PBMCs) of patients who recovered from DENV-1 infection were infected with DENV-1 or DENV-2 and co-cultured with memory T cells. We found that secondary infection with DENV-2 suppresses the cell reproductive capacity but forms more cell clones and more functional cells to produce more proinflammatory factors (IFN- $\gamma$ , TNF- $\alpha$ , IL-6, IL-8, IL-12 and IL-17) and less regulatory cytokines (IL-10, TGF- $\beta$ ) which results in higher viral replication compared to secondary infection with DENV-1. Memory dengue virus-specific T cells which are induced in a primary dengue virus infection are reactivated by the heterologous serotype of dengue virus and antigen-presenting cells (APCs) during a secondary infection. Dramatically, less apoptosis and more continuous activation of T cells in secondary infection with hetero-serotype DENV were observed. This discovery which has not been reported previously may be the reasonable and vital interpretation for the cytokine storm and severe symptoms observed in secondary infection with DENV. In summary, secondary infection with hetero-serotype DENV elicits the relatively pathological immune response while secondary infection with homologous-serotype DENV induces the relatively protective immune response by activation-induced cell death (AICD) of T cells.

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**PREDISPOSING SECOND IN ADULT DENGUE PATIENTS**

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Dengue, a major public health problem in the world, is now endemic in more than 100 countries. It is estimated to have 390 million Dengue infections with 96 million cases worldwide. Mortality rate can be high ranging from 0.1% to 5%. Bleeding is a common complication in Dengue which can even lead to death if not detected and treated early. Therefore, identifying predictors of bleeding would be very valuable as such patients could be closely monitored to detect and treat bleeding early. A prospective Case Control Study was conducted to determine the incidence of bleeding, type of bleeding and possible predictors of bleeding. All patients admitted to Dengue Management Unit at the National Institute of Infectious Diseases, Colombo, Sri Lanka for a period of four months from 1st of July 2014 were included in the study. Dengue infection was confirmed by NS1 antigen or Dengue Specific IgM antibodies. These patients were followed up to see the development of bleeding, possible effects of bleeding and the need of blood transfusion. There were 1000 patients with confirmed Dengue infection with 546 males and 454 females. Age ranged from 12 to 86 years. (mean 31 yrs.) 56.2% (n=562) had DF; 43.8% (n= 438) had DHF. 332(33.2%) had some degree of bleeding; major bleeding in 17.0%, minor bleeding in 15.9%; 67.1% had no bleeding at all, other than petechial bleeding. 81(8.1%) needed therapeutic blood transfusions. Major bleeding was significantly more common (p<0.05) in those who had severe vomiting, postural dizziness, abdominal pain and hepatic tenderness and those who had NSAIDS. Females had more bleeding than men (p<0.05). Obese patients had a higher risk of having bleeding (p<0.05), but not overweight patients(BMI 23-27). Patients with platelet counts less than 50,000 per cmm were at a higher risk of having bleeding as well as DHF patients. This study identifies

predictors which would put Dengue patients at high risk of bleeding. This will enable clinicians to monitor such patients carefully to detect and to treat bleeding promptly thereby reducing morbidity and mortality.

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**PREVALENCE OF DENGUE AND CHIKUNGUNYA VIRUS INFECTIONS IN NORTHEASTERN TANZANIA: A CROSS SECTIONAL STUDY AMONG PARTICIPANTS PRESENTING WITH MALARIA-LIKE SYMPTOMS**

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Abstract In spite of increasing reports of dengue and chikungunya activity in Tanzania, limited research has been done to document the general epidemiology of dengue and chikungunya in the country. This study aimed at determining the sero-prevalence and prevalence of acute infections of dengue and chikungunya virus among participants presenting with malaria-like symptoms in three communities with distinct ecologies of north-eastern Tanzania. Cross sectional studies were conducted among 1100 participants (aged 2-70 years) presenting with malaria-like symptoms at health facilities at Bondo dispensary (Bondo, Tanga), Hai hospital (Hai, Kilimanjaro) and TPC hospital (Lower Moshi). Participants who were malaria negative using rapid diagnostic tests (mRDT) were screened for sero-positivity towards dengue and chikungunya Immunoglobulin G and M using ELISA-based kits. Participants with specific symptoms defined as probable dengue and/or chikungunya by WHO were further screened for acute dengue and chikungunya infections by PCR. Out of a total of 1100 participants recruited, 91.2% (n=1003) were malaria negative by mRDT. Out of these, few of the participants (<5%) were dengue IgM or IgG positive. A total of 381 participants had fever out of which 7.9% (30/381) met the defined criteria for probable dengue, though none (0%) was confirmed to be acute cases. Chikungunya IgM positives among febrile participants were 12.9% (49/381) while IgG positives were at 3.7% (14/381). A total of 69.0% (263/381) participants met the defined criteria for probable chikungunya and 4.2% (11/263) were confirmed by PCR to be acute chikungunya cases. Further analyses revealed that headache and joint pain were significantly associated with chikungunya IgM seropositivity. In north-eastern Tanzania, mainly chikungunya virus appears to be actively circulating in the population. Continuous surveillance is needed to determine the contribution of viral infections of fever cases. A possible establishment of arboviral vector preventive control measures and better diagnosis of pathogens to avoid over-treatment of other diseases should be considered.

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**NATURAL ANTIBODY RESPONSES TO THE CAPSID PROTEIN OF DENGUE**

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The capsid (C) protein is a structural protein of the dengue virus (DENV) that encloses its genetic material. Few previous studies reported antibody responses to DENV C protein during natural infection. To further understand this, we studied natural antibody responses against C protein of all four DENV serotypes. Antibody responses of sera obtained from dengue seropositive healthy volunteers (DENV1 n=8: DENV2 n=8: DENV3 n=5 and DENV4 n=8) from Sri Lanka, were screened against an array of 14 peptides, representing the entire C protein sequence of DENV2, using