

**MOLECULAR UNDERSTANDING OF DENGUE VIRUS PATHOGENESIS AMONG
EASTERN INDIAN PATIENTS AND DETERMINATION OF EFFECT OF QUERCETIN
AGAINST DENGUE**

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ABSTRACT

Currently Dengue virus (DENV) infection has been one of the major public health problems, ranging from self limiting mild febrile illness to severe and fatal disease outcome (DHF/DSS). Pathophysiology of severe dengue is still unclear, viral factors and host immune response might play crucial role in determining disease severity. In India, scenario has been found to be very much complex and also frequently changed in each outbreak in terms of severity of the disease. Currently, there are no prognostic markers which could predict disease severity of dengue infected patients and no anti-viral therapy is currently available that could inhibit DENV replication at early stage of infection. Hence, this study aimed to evaluate importance of viral factors viz. circulation serotypes, viral load; and host factors: immunogenetic make up of host innate immune genes viz. polymorphic variants of toll like receptors (TLR3, 7, and 8), C-reactive protein (CRP) and serum protein levels in determining disease susceptibility and severity. Identification of reliable dengue severity predictive markers in patient serum and evaluation of antiviral effect of Quercetin, a plant derived bioactive compound, against DENV replication will be helpful in dengue disease management.

In this study, total 51.5% (309/600) patients were found to be dengue infected. Among the circulating serotypes, D2 and D2-D4 were most predominant mono and co-infected serotypes of which D2 serotype was also found to be more prevalent among severe dengue patients. Non-synonymous polymorphisms of TLR7 [rs179008 (gly111leu)] and TL8 [rs3764880 (met1val)] genes were found to be associated with disease susceptibility and severity. The TT genotype of CRP polymorphism rs3091244 was found to be significantly associated with disease susceptibility, severity, high viral load and increased concentration of CRP. Serum levels of endothelial markers viz. Ang2, VEGF, acute phase protein - Apo A1 and hepatic markers viz. AST and ALT can predict dengue disease severity at early stage of infection with high sensitivity and specificity with severity cut values of Ang2: 1129 pg/ml (AUC: 0.97), VEGF: 526 pg/ml (AUC: 0.99), Apo A1: 23.18 (AUC: 0.93), AST: 227.3 IU/L (AUC: 0.99) and ALT: 205 IU/L (AUC: 0.99), respectively. Quercetin significantly minimized DENV copy number, vascular leakage, concentration of inflammatory cytokines viz. TNF α and IL-6, intra cellular ROS response and histopathological hepatic alterations in DENV infected Balb/C mice compared to dengue-infected mice and thus, reflected it's therapeutic and immunomodulatory potential against dengue virus.

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