

Dengue Fever : It's Ever - Changing and Elusive Predictors of Severity

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Dengue fever (DF), a mosquito-borne disease, with an estimated infection rate of about 390 million infections per year, affects nearly half of the global population residing in dengue-endemic areas. [1]

The first epidemics of dengue-like illness, diagnosed clinically, occurred simultaneously in Asia, Africa, and North America in the 1780s, including reports from Madras, India. Following the isolation of dengue virus in 1943 by scientists, during the dengue epidemic in Nagasaki, Japan, the first major epidemic of the Dengue Hemorrhagic Fever (DHF) occurred in 1953-1954 in Philippines. Thereafter, there was rapid global spread of epidemics of DF/DHF. Further, it has been documented that the four closely related dengue viruses - DEN-1, DEN-2, DEN-3 and DEN-4 causing DF are found in the same regions of the world. [2]

India reported its first virologically confirmed epidemic of dengue fever from Calcutta and Eastern Coast of India in 1963-1964. [3] The country experienced major wide spread epidemics of DHF and Dengue Shock Syndrome in 1996, involving areas around Delhi and Lucknow following which, the infection spread to the entire country. [4] Currently, India contributes to nearly 34% of the global dengue burden with over a lakh case occurring even in this current year (2021). [5]

Unplanned urbanisation, changing rainfall patterns and delayed preventive measures have facilitated mosquitoes to thrive. Not only does the infection pose serious challenges for the administration, it also creates a tough situation for the physicians, who have to fight the virus without the availability of specific drugs or preventable vaccines.

Although majority of infected individuals remain asymptomatic or experience a benign febrile illness, a minority develop severe dengue which is life-threatening. The progression to severe disease commonly occurs after the febrile phase. To enable clinicians in the early detection of severe disease progression, some warning signs were enumerated in the 2009 WHO dengue guidelines as early indicators of plasma leakage. [6] Although these warning signs have high sensitivity in identifying those at high risk, their non-specific nature leads to unnecessary admissions,

during the dengue season. [7]

A number of studies have been done to identify factors associated with early onset of plasma leakage. Systematic reviews and meta-analyses [8] collating these studies have found high heterogeneity in the clinical factors associated with disease progression. A recent systematic review, published in 2021, by Sangkaew, et al. [9] synthesizing a total of 150 articles, more than 80% of which were from Asia and Latin America, provides useful information regarding early prognostic factors associated with severe disease progression, for effective risk-stratification and monitoring of patients. Regarding demographic and co-morbid factors, the meta-analysis showed that older adults and younger children, pre-existing diabetes, hypertension, renal or cardiovascular disease were significantly associated with progression to severity. Of all the clinical features, the ones which predicted high risk of severity included vomiting, abdominal pain and tenderness, bleeding and pleural effusion or ascites. Laboratory parameters, namely, platelet count, transaminases and serum albumin were found to be independent predictors of progression to severe dengue. Interestingly, the meta-analysis found that neither total leukocyte count nor hematocrit could predict severe dengue. Further, rather than the viral load, it was the serotype 2 of Dengue virus which was associated with severe disease in children.

This issue of the journal provides insight regarding this relevant topic, through an original study from India, describing 150 children, between 2 months and 12 years of age, hospitalized with dengue. [10] The prospective study analyses the risk factors for severe dengue and mortality which occurred in 14% and 0.05%, respectively, of the entire cohort. A better understanding of these factors will help clinicians to identify high-risk patients and take effective measures promptly to prevent complications and mortality in dengue fever.

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