

Microvascular and endothelial function for risk prediction in dengue: an observational study

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Abstract

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Background Dengue infection can result in a wide spectrum of disease. The defining feature of severe disease is increased capillary permeability, which can lead to hypovolaemic shock. Microvascular and endothelial dysfunction might underlie hypovolaemic shock, but they have not been assessed clinically. We aimed to investigate the use of microvascular assessment as a prognostic method in dengue.

Methods This is an ongoing prospective observational study that aims to recruit 300 participants: children over the age of 3 years and adults presenting to two outpatient departments in Vietnam with fever of less than 72 h duration and suspected dengue, and patients admitted to hospital with warning signs or severe disease. Participants are being clinically assessed daily for 6 days, and 2 weeks later. Microvascular imaging using sublingual sidestream darkfield imaging (SDF) and endothelial function testing using peripheral artery tonometry are being performed at enrolment, defervescence, and follow-up

Findings To date, 167 patients have been recruited (92 outpatient arm, 75 inpatient arm, median age 27 years [IQR 21–33], 78 male [47%]). Dengue has been confirmed in 67 individuals in the outpatient arm, of whom 29 (43%) developed warning signs, three (4%) developed severe disease, and 35 had uncomplicated dengue; the other 25 outpatients (27%) were diagnosed as other febrile illness. At enrolment, the reactive hyperaemic index, a marker of endothelial function, was lowest in the patients who went on to develop severe dengue (median 1.54, IQR 1.36–1.77) followed by those who developed warning signs (1.78, 1.43–2.36) and then uncomplicated dengue (2.18, 1.65–2.24). Initial SDF results showed a lower proportion of perfused vessels and mean flow index during the febrile phase of dengue compared with follow-up, and were worst in the severe group at defervescence.

Interpretation This study of vascular function at serial timepoints in dengue is, to our knowledge, the first and most comprehensive. Our preliminary results suggest that microvascular and endothelial dysfunction are associated with severity of dengue, and occur before the appearance of severe clinical manifestations. These techniques might be useful in risk prediction in dengue. A limitation is that a formal sample size could not be calculated because no previous microvascular data in dengue exist.

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Contributors

SY, HW, GS, BW, and CPS designed the study. SY wrote the abstract. All authors have read and approved the final version.

Declaration of interests

We declare no competing interests.