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Increased serum nitrite levels and low serum IgM levels in severe dengue (dengue hemorrhagic fever) patients

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Identification of dengue hemorrhagic fever (DHF) at an early stage of the disease could unravel many issues in clinical management of severe dengue. Thus, the main objective of this study is to seek the prognostic value of Serum nitrite, a secondary stable intermediate of nitric oxide in severe (DHF) and mild dengue fever (DF) patients along with its association with serum IgM antibody levels. Clinically confirmed DHF (n=40) and DF (n=60) patients were selected from Colombo North Teaching hospital (CNTH), Ragama, excluding patients with previous dengue episodes and other infectious and non-infectious diseases**.** Blood samples were collected at different stages of disease; admission (A), critical (C) and discharge (D). Disease was confirmed by detection of NS1 antigen and IgM levels were measured using commercially available quantifying ELISA kit. Griess assay was carried out for deproteinized sera to seek the nitrite levels. Results showed significantly higher serum nitrite level in DHF-A (mean ± SD, 1.535 ± 0.705 µM) compared to DF-A (1.240 ± 0.475 µM, independent sample t test, p=0.027). ROC curve analysis between DF-A and DHF-A showed 62.6% area under the curve (p=0.036). Cut off value for serum nitrite in DHF-A was determined as 1.255 µM with 63.9% sensitivity and 60.5% specificity. Moreover, DHF-A has significantly higher nitrite value compared to DHF-D (paired sample t test, p=0.006). Thus, these results postulate that high levels of nitrite in DHFA may be due to high production of nitric oxide associated with pathogenesis of severe dengue and higher expression of inducible nitric oxide synthase enzyme (iNOS). Analysis of IgM revealed significantly higher levels of antibodies in DF (75.71 ± 47.42 U/ml) compared to DHF (52.21 ± 36.20 U/ml) (p=0.045) patients, implying IgM may be playing a protective role in DF. However, no significant association was obtained between IgM and nitrite levels in each patient category. Nevertheless, other studies have shown that in severe dengue, antibodies produced against NS1 antigen could bind endothelial cells which enhance the release of nitric oxide causing cell apoptosis. Lack of association between IgM and nitrite levels observed here indicate that there may be other mechanisms contributing to DHF.

Keywords: Dengue hemorrhagic fever, reactive nitrogen species, IgM antibodies, prognostic markers, pathogenesis

Acknowledgement: National Science Foundation, Grant No. RG/2014/HS/04

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