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Higher incidence of stroke in patients with dengue fever: Spurious association or causal link?

Nguyen Tien Huy^{1*}, Sedighe Karimzadeh², and R Matthew Chico³

A recently published population-based cohort study by Li and colleagues (1) suggests that stroke patients in Taiwan were 2.49 times more likely to have been diagnosed with dengue infection in the preceding two months relative to paired controls. Although rare, dengue-associated stroke does meet the criteria for severe dengue diagnosis based on guidelines from the World Health Organization (2). Li and colleagues report an overall increase in the incidence of stroke attributable to dengue by 1.61 per 1000 person-years during 2015. If these findings are extended to all 43,419 cases of dengue across Taiwan in 2015 (3), then 70 cases of stroke would have occurred due to dengue infection. This is alarming, particularly considering that there are 96 million cases of symptomatic dengue each year worldwide (4). Have the authors identified a spurious association, or is there a genuine causal link between dengue and stroke? Co-morbidity of dengue and hemorrhagic stroke have been reported in 0.26% of cases (3 of 1,148) in India (5), and 0.06% of cases (1 of 1,585) in Brazil (6).

Rigorous research is urgently needed to characterise the sequelae of conditions that may arise from dengue infection, including the severity and duration of underlying disease such as diabetes mellitus and hypertension, conditions that may modify the effect of dengue on the risk of stroke. If the effect of dengue on stroke is acute rather than chronic, then there must be a pathophysiologic mechanism involved. Severe dengue diagnosis under the new classification system presents different and potentially unrelated mechanisms of action (7). In short, more clinical data are needed to support the results of Li and colleagues.

¹ Nguyen Tien Huy, MD, PhD, Associate Professor, Department of Clinical Product Development, Institute of Tropical Medicine, Nagasaki University, Japan

² Sedighe Karimzadeh, School of Medicine, Sabzevar University of Medical Sciences, Iran

³ R Matthew Chico, MPH, PhD, Assistant Professor of Public Health, Department of Disease Control, Faculty of Infectious & Tropical Diseases, London School of Hygiene & Tropical Medicine, United Kingdom

* Corresponding author

References

1. Li H-M, Huang Y-K, Su Y-C, Kao C-H. Risk of stroke in patients with dengue fever: a population-based cohort study. *Canadian Medical Association Journal*. 2018;190(10):E285-E90.

2. World Health Organization. Dengue guidelines for diagnosis, treatment, prevention and control: new edition. 2009.
3. Wang S-F, Chang K, Loh E-W, Wang W-H, Tseng S-P, Lu P-L, et al. Consecutive large dengue outbreaks in Taiwan in 2014–2015. *Emerging microbes & infections*. 2016;5(12):e123.
4. Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, et al. The global distribution and burden of dengue. *Nature*. 2013;496(7446):504-7.
5. Mathew S, Pandian JD. Stroke in patients with dengue. *Journal of Stroke and Cerebrovascular Diseases*. 2010;19(3):253-6.
6. Souza Ljd, Martins ALdO, Paravidini PCL, Nogueira RMR, Gicovate Neto C, Bastos DA, et al. Hemorrhagic encephalopathy in dengue shock syndrome: a case report. *Brazilian Journal of Infectious Diseases*. 2005;9(3):257-61.
7. Srikiatkachorn A, Rothman AL, Gibbons RV, Sittisombut N, Malasit P, Ennis FA, et al. Dengue—how best to classify it. *Clinical Infectious Diseases*. 2011;53(6):563-7.