



Clinicopathological Profile and Incidence of Dengue and Relative Bradycardia

Dr. MAHESH PAL KHATRI	Assistant Prof. Medicine Department of Medicine, Sardar Patel Medical College & P.B.M. Hospital Bikaner, Rajasthan Rajasthan.
Dr. ROHITASH KULARIA	Assistant Prof. Medicine Department of Medicine, Sardar Patel Medical College & P.B.M. Hospital Bikaner, Rajasthan Rajasthan.
Dr. VIJAYTA MODI	Senior Demonstrator, Pathology Department of Pathology, Sardar Patel Medical College & P.B.M. Hospital Bikaner, Rajasthan Rajasthan.
Dr. ANITA SHARMA	Assistant Prof. Obst. & Gynae Department of Obst. & Gynae, Sardar Patel Medical College & P.B.M. Hospital Bikaner, Rajasthan Rajasthan.

ABSTRACT

Relative bradycardia has been reported in many infectious diseases, including typhoid fever, Legionnaires' disease, psittacosis, typhus, leptospirosis, malaria, and babesiosis (5,6). During the 2015 India outbreak, we observed relative bradycardia in several patients with dengue fever. We therefore performed a case-control study comparing febrile dengue patients to patients with other infectious diseases. The study was approved by our hospital's ethics committee. The records of all patients admitted with a febrile illness to general medical unit from January 1 to December 31, 2015, were reviewed. Patients with a clinical diagnosis of dengue fever and serologic confirmation (IgM or PCR positive) plus a temperature $>38^{\circ}\text{C}$ were included as case patients. Age-matched controls were selected from the same general medical inpatient units and were admitted during the same period. Inclusion and exclusion criteria were strictly followed. The mean age (\pm standard deviation) for dengue patients was 32.8 (± 10.8) years and for controls was 36.5 (± 10.2) years ($p = 0.08$). There were 39 male patients in the dengue group and 31 in the control group. Their mean peak temperatures were comparable: 38.6°C (± 0.5) (dengue) and 38.8°C (± 0.7) (controls) ($p = 0.09$). Mean heart rates were significantly lower in the dengue group: 87.6 (± 12.5) beats/min (dengue) and 104.6 (± 14) beats/min (controls) ($p < 0.0001$). The heart rates at peak temperatures for patients with dengue fever were compared with rates for controls at all temperatures. Our findings demonstrate a consistently lower heart rate at all peak temperatures recorded ($p < 0.0001$). Further studies could consider the relative importance of immune and neural mechanisms and also any direct cardiac pathology in the etiology of dengue-associated relative bradycardia.

KEYWORDS

Dengue, Relative bradycardia

Introduction:

Dengue fever is a potentially fatal illness; >2.5 billion persons are at risk and the disease is endemic in almost 100 countries (1). India recorded $>14,000$ cases in 2015, its highest annual figure (2). No specific clinical features distinguish dengue from other febrile illnesses (3); thus, diagnosis relies heavily on results of laboratory investigations. Virus-specific immunoglobulin M (IgM) antibodies only become detectable after 5–7 days, and false-positive results can confound the diagnosis. PCR is a useful diagnostic tool; however, it is limited by the short duration of viremia and requirements for sophisticated laboratory support (4). Relative bradycardia has been reported in many infectious diseases, including typhoid fever, Legionnaires' disease, psittacosis, typhus, leptospirosis, malaria, and babesiosis (5,6).

Material and Method:

During the 2015 India outbreak, we observed relative bradycardia in several patients with dengue fever. We therefore performed a case-control study comparing febrile dengue patients to patients with other infectious diseases. The study was approved by our hospital's ethics committee. The records of all patients admitted with a febrile illness to general medical unit from January 1 to December 31, 2015, were reviewed. Patients with a clinical diagnosis of dengue fever and serologic confirmation (IgM or PCR positive) plus a temperature

$>38^{\circ}\text{C}$ were included as case patients. Age-matched controls were selected from the same general medical inpatient units and were admitted during the same period. All had fever, but they had a proven alternative diagnosis, including pneumonia (12 patients), upper respiratory tract infection (9 patients), urinary tract infection (6 patients), tuberculosis, liver abscess, viral fever other than dengue (3 patients each), meningitis, chickenpox, cellulitis, typhoid fever (2 patients each), and appendicitis, psoas abscess, typhus, infective endocarditis, pressure ulcers, and gastroenteritis (1 patient each). Exclusion criteria were the following: no laboratory confirmation, age >60 years, preexisting substantial heart or lung disease or concurrent medication affecting heart rate, e.g., β -blockers, α -agonists, calcium channel blockers, or xanthine derivatives. The peak temperature of all case patients and controls was recorded within the first 24 hours of admission as well as heart rate and blood pressure at that point. Leukocyte count, hemoglobin concentration, hematocrit, and platelet counts were also noted.

Results:

Data from 50 case-patients and 50 controls were tabulated and analyzed with Microsoft Excel (Microsoft Corp., Redmond, WA, USA). The mean age (\pm standard deviation) for dengue patients was 32.8 (± 10.8) years and for controls was 36.5

(± 10.2) years ($p = 0.08$). There were 39 male patients in the dengue group and 31 in the control group. Their mean peak temperatures were comparable: 38.6°C (± 0.5) (dengue) and 38.8°C (± 0.7) (controls) ($p = 0.09$). Mean heart rates were significantly lower in the dengue group: 87.6 (± 12.5) beats/min (dengue) and 104.6 (± 14) beats/min (controls) ($p < 0.0001$).

Electrocardiographs (ECGs) were available for 10 of the dengue group, and all showed normal sinus rhythm. Three patients with bradycardia had an ECG. Results for 2 patients were normal; 1 showed mitral valve prolapse with mild regurgitation. Ten patients in the control group underwent an ECG, and none had any notable abnormality. Four controls had ECGs, results for 2 were normal; 1 had mild mitral regurgitation, and 1 had mild tricuspid regurgitation. The heart rates at peak temperatures for patients with dengue fever were compared with rates for controls at all temperatures. Our findings demonstrate a consistently lower heart rate at all peak temperatures recorded ($p < 0.0001$).

Discussion:

Dengue fever may adversely affect cardiac function. An echocardiographic study by Khongphatthanayothin et al.⁽⁷⁾ showed depressed myocardial contractility and suboptimal heart rate response in some patients with dengue hemorrhagic fever. Acute reversible hypokinesia and reduction in left ventricular ejection fraction was also reported by Wali et al.⁽⁸⁾. The underlying mechanisms were postulated to be immune in origin, although myocarditis may be a contributory factor. Fever production in response to exogenous pyrogens is believed to be mediated mostly by cytokine prostaglandin pathways, and neural input is important in the early phases of fever⁽⁹⁾. Concentrations of cytokines, including tumor necrosis factor, interferon- γ , interleukin-8 (IL-8), IL-10, and IL-12, are substantially increased during dengue infection. Their levels likely correlate with specific clinical manifestations and illness severity⁽¹⁰⁾. The relationship of cytokines to relative bradycardia is unknown.

Conclusion:

Further studies could consider the relative importance of immune and neural mechanisms and also any direct cardiac pathology in the etiology of dengue-associated relative bradycardia.

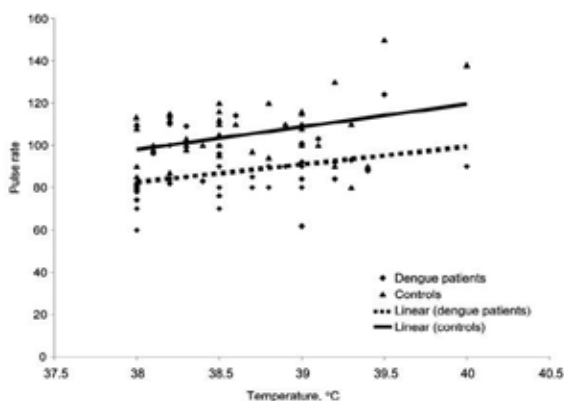


Figure. Temperature and heart rate relationship: scatter plot for patients with dengue fever and nondengue febrile illnesses

REFERENCES

- Guzman MG, Kouri G. Dengue: an update. *Lancet Infect Dis.* 2002;2:33–42.
- Agarwal D. To the vector borne...mosquitotransmitted diseases in India, IJVD. 2015;11:96.
- Wilder-Smith A, Earnest A, Paton NI. Use of simple laboratory features to distinguish the early stage of severe acute respiratory syndrome from dengue fever. *Clin Infect Dis.* 2004;39:1818–23.
- Guzman MG, Kouri G. Dengue diagnosis, advances and challenges. *Int J Infect Dis.* 2004;8:69–80.
- Ostergaard L, Huniche B, Andersen PL. Relative bradycardia in infectious diseases. *J Infect.* 1996;33:185–91.
- Cunha BA. The diagnostic significance of relative bradycardia in infectious disease. *Clin Microbiol Infect.* 2000;6:633–4.
- Khongphatthanayothin A, Suesaowalak M, Muangmingsook S, Bhattarakosol P, Panchareon C. Hemodynamic profiles of patients with dengue hemorrhagic fever during toxic stage: an echocardiographic study. *Intensive Care Med.* 2003;29:570–4.
- Wali JP, Biswas A, Chandra S, Malhotra A, Aggarwal P, Handa R, et al. Cardiac involvement in dengue haemorrhagic fever. *Int J Cardiol.* 1998;64:31–6.
- Blatteis CM, Li S, Li Z, Feleider C, Perlik V. Cytokines, PGE2 and endotoxic fever: a reassessment. *Prostaglandins Other Lipid Mediat.* 2005;76:1–18.
- Fink J, Gu F, Vasudevan SG. Role of T cells, cytokines and antibody in dengue fever and dengue haemorrhagic fever. *Rev Med Virol.* 2006;16:263–75.