

Nationwide prevalence of *Rickettsia felis* infections in patients with febrile illness in Bangladesh

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Abstract

From July 2015 to December 2016, the presence of rickettsial pathogens was investigated for 414 patients with unknown fever in eight places in all the divisions of Bangladesh. *Rickettsia felis* was identified in blood samples from all the regions (overall detection rate, 19.6%), suggesting nationwide prevalence of *R. felis* infections. © 2017 The Author(s). Published by Elsevier Ltd.

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Rickettsia felis is an obligate intracellular bacterium belonging to the transitional group Rickettsiae, and causes febrile disease known as cat-flea typhus [1–3]. Transmission of *R. felis* to humans is mediated by cat fleas from an unknown reservoir; mosquitoes are also suspected of being potential vectors [2,4].

Since the first report in the USA in 1994 [5], *R. felis* infection has been spreading as an emerging infectious disease globally, but frequencies of genetically confirmed cases were very low in Asian countries [1,2,6]. However, in our previous studies in central-northern Bangladesh (Mymensingh), *R. felis* DNA was identified in blood samples from febrile patients at a high rate (46% in 2012/13 [7], 42% in 2013/14 [8]), which indicated the significance of studying the prevalence of *R. felis* infections in other parts of Bangladesh. Hence, we conducted an extended cross-sectional study covering all regions in Bangladesh, to determine the overall prevalence of *R. felis* infection, and to explore any difference in its prevalence depending on region.

A total of 414 blood samples from febrile patients (sex ratio, 0.89; age range, 7 months to 73 years) (see Supplementary material, Tables S1 and S2) were obtained in the collaborative medical institutions located in all eight divisions in Bangladesh (Dhaka, Rangpur, Rajshahi, Mymensingh, Sylhet, Khulna, Barisal and Chittagong) (Fig. 1) during a period from July 2015 to December 2016. Inclusion criteria for patients were the same as that employed in our previous study [7], including the positive Weil–Felix test ($\geq 1:160$ titre) (see Supplementary material, Table S3). This study was approved by the Institutional Review Board, and informed consent was taken from individual patients (or guardians). Through nested PCR and sequencing of the PCR product as described previously [5,7], the 17-kDa antigen gene of *R. felis* (strain URRWXC12, GenBank Accession no. CP000053) was identified in 81 samples, representing an overall detection rate of 19.6%. Among them, 26 and 15 samples were PCR positive for 16S rRNA gene and *gltA*, respectively, showing identical sequences to those of *R. felis* strain URRWXC12. Detection rates of *R. felis* were different depending on the study site: Dhaka, 24%; Rangpur, 36%; Rajshahi, 30%; Mymensingh, 20%; Sylhet, 5%; Khulna, 3%; Barisal, 24%; Chittagong, 10% (Fig. 1). *Rickettsia typhi* was identified in only one sample, from Barisal, and had 17 kDa antigen gene, 16S rRNA gene and *gltA* sequences identical to those of *R. typhi* strain Wilmington (GenBank Accession no. AE017197). Among all the *Rickettsia*-positive patients (age and sex distribution; see Supplementary material, Tables S4 and S5), OX-2 showed the highest positive rate (74%; solely OX-2-positive, 50%) in the Weil–Felix test (see Supplementary material, Table S6). None of these patients had malaria, typhoid fever or brucellosis, whereas dengue and chikungunya had not been tested.

The present study revealed the nationwide prevalence of *R. felis* infections in Bangladesh. It was noted that higher detection rates of *R. felis* were observed in central regions including Dhaka, and northwest regions (Rangpur and Rajshahi), although sufficient numbers of samples were not available in some study sites. Recent serological studies in Bangladesh also

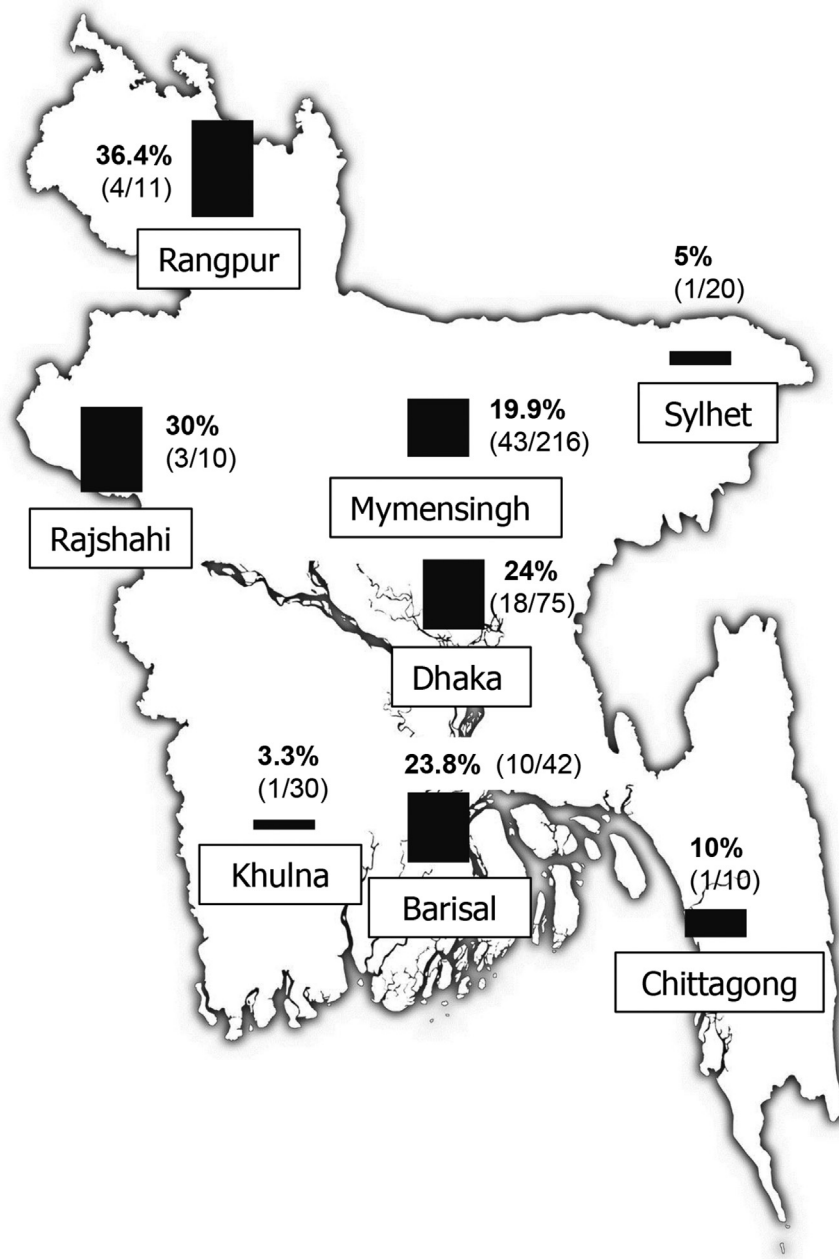


FIG. 1. Geographical locations of the eight study sites in Bangladesh. Height of filled bar represents relative value of *Rickettsia felis* positive rate (%) as shown. Numbers of *R. felis* positive samples / total samples examined are indicated in parentheses.

described higher prevalence of *R. typhi* in Dhaka and Comilla (eastern district) [9], and spotted fever group rickettsiosis and scrub typhus in Rajshahi [10]. Accordingly, it is suggested that the geographical distribution of *R. felis* in Bangladesh may be similar to those of other rickettsial pathogens. Apparent difference in the prevalence of *R. felis* by study site may be related to number of cats/dogs associated with population and its density in individual divisions, although a definite reservoir of this *Rickettsia* has not yet been established. Recently, detection of *R. felis* DNA was reported in the *Anopheles gambiae* mosquito [4], and also in blood and skin of healthy individuals [6,11,12],

suggesting a capability of *R. felis* to colonize or infect various living organisms. Therefore, further studies are necessary to determine definite pathogenic significance of *R. felis* DNA in humans, and also to explore the potential reservoir and vector of this bacterium, in a putative endemic area such as Bangladesh.

Transparency declaration

The authors have no conflicts of interest to declare.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.nmni.2017.07.005>.

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