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Letter to the Editor

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Possible Drivers of the 2019 Dengue Outbreak in Bangladesh: The Need for a Robust Community-Level Surveillance System

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Bangladesh experienced its largest dengue virus (DENV) outbreak in 2019, with 101,354 patients admitted to hospital with either laboratory-confirmed or clinical diagnosis. By contrast, the cumulative number of dengue patients admitted to hospitals in the previous 19 yr (2000–2018) was 50,674 (Institute of Epidemiology Disease Control and Research 2019). Herein, we discuss the potential drivers contributing to the unprecedented 2019 DENV outbreak in Bangladesh.

Dengue fever is caused by four serotypically distinct dengue viruses (DENV-1 to DENV-4) that are transmitted by *Aedes* spp mosquitoes. Infection with one serotype does not protect against another, except for the first few months after infection (Sabin 1952). Since 2000, Bangladesh has reported DENV cases every year before the 2019 surge (Fig. 1). However, under-reporting was highly likely because previous reports only included data from a select number of government hospitals and private clinics (Directorate General of Health Services [DGHS] 2019, Mamun et al. 2019). The number of dengue patients reported by the Institutes of Epidemiology Disease Control and Research (IEDCR), a research wing of the Ministry of Health and Family Welfare, includes patients from in-patient departments of 12 government or autonomous hospitals and 29 of 609 private hospitals (Bangladesh Private Clinic Diagnostics Owners Association: http://www.bpcdoa.com/about_us.html). Dengue cases were identified based on clinical symptoms (including fever and rash) and/or laboratory tests for IgM or IgG antibodies to DENV, and nonstructural 1 protein (NS-1) of DENV (Diseases Control Division (DGHS) 2013). Nevertheless, data on asymptomatic infections or patients that developed mild symptoms and did not seek medical attention were unknown and were not included in these data.

We suggest three primary reasons for the large outbreak of dengue in 2019: 1) introduction of a new serotype (DENV-3) into a largely naïve population, 2) an unusually wet pre-monsoon season which provided two additional months of mosquito reproduction, and 3) resistance to insecticides. In Bangladesh, all four serotypes of DENV have been detected (Table 1), with DENV-3 as the predominant virus until 2002 (Pervin et al. 2003). IEDCR's surveillance identified DENV-3 in Dhaka City again in 2017 (Institute of Epidemiology Disease Control and Research 2019, Shirin et al. 2019). This virus caused a moderate outbreak in 2018 (Shirin et al. 2019), but probably reached peak prevalence the subsequent year, 2019, when DENV-3 was the predominant DENV circulating in the country (Table 1) (Institute of Epidemiology Disease Control and Research 2019). A nationally representative serological study detected 24% seropositivity, with >80% prevalence in Dhaka City and 3% in the northern part of the country. This survey was conducted during 2015–2016 when DENV-1 and DENV-2 were circulating in the country. The absence of DENV-3 for 16 yr (since 2002) provided a large population susceptible to this serotype: almost an entire generation of non-DENV-3 immune individuals primed for antibody enhancement of infection by other serotypes as well as those with waned DENV-3 immunity. Thus, the circulation of DENV-3 in 2019 contributed to a major epidemic in the country. Concurrently DENV-3 was circulating in neighboring India (Parveen et al. 2019) and multiple countries in South East Asia, including Thailand (Hamel et al. 2019), with whom Bangladesh has a strong trade/travel links.

The second plausible reason for the increase in cases was the unusually high rainfall before the normal 2019 monsoon season. In Bangladesh, the dry season extends from November to February, when rainfall is typically very rare. However, during 2019 a record 120 ml rainfall was documented during February in Dhaka City by the Bangladesh Meteorological Department, the highest rainfall for that month during the 2000–2019 period (mean 15 ml [range: 0–56]) (Fig. 2). After that initial heavy rainfall, intermittent to heavy rainfall continued until October 2019. Therefore, the vector season started earlier compared to previous years, which may have triggered early-season *Aedes* population growth and DENV transmission until the end of the year. We performed the Mann-Kendell trend analysis for annual mean rainfall data collected from the Bangladesh Meteorological Department between 2000 and 2019 and failed to observe any significant

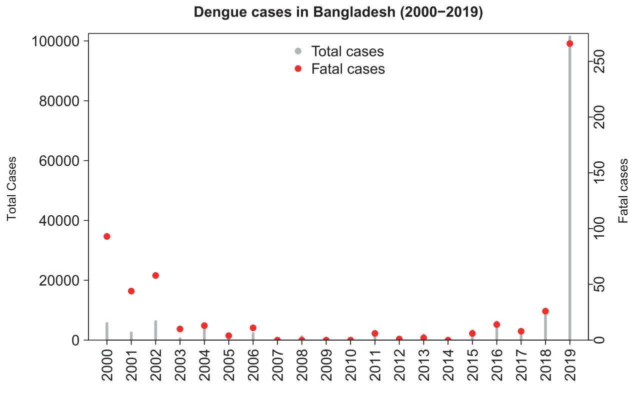

Fig. 1. The number of total (gray symbol) and fatal (black symbol) dengue cases in Bangladesh between 2000 and 2019. Note the different scales on the two *y*-axes. The number of dengue cases detected in 2019 was more than double the cumulative number of cases detected in the previous 19 yr.

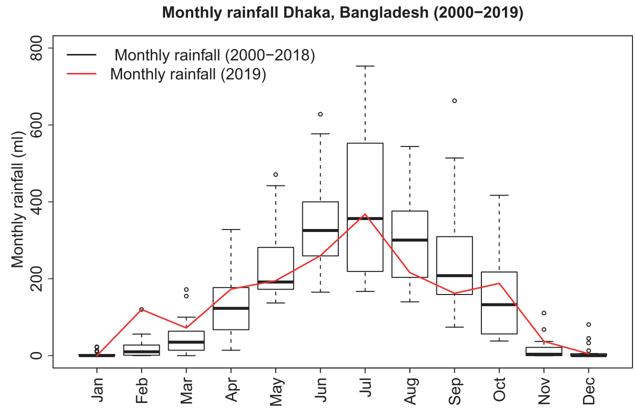

Fig. 2. The monthly rainfall in Dhaka recorded by the Bangladesh Meteorological Department, 2000–2019. The boxplot (in black) represents the amount of rainfall in Dhaka from 2000 to 2018, whereas the red line indicates the mean rainfall in 2019. During 2019, the rainfall started early and lasted longer than the usual monsoon period. The bottom and top of the box indicate the first and third quartiles of rainfall, respectively; the band inside the box is the median value, and the whiskers show the lowest and highest data points within 1.5 times the interquartile range of the respective lower and upper quartiles. The dots outside the box are outliers (for color figure refer online version).

Table 1. The serotypes of DENV circulating in Bangladesh since 2013 (Adapted from Bangladesh's Institute of Epidemiology Disease Control and Research [IEDCR]; Institute of Epidemiology Disease Control and Research 2019)

Years	Serotypes of DENV
2013–2016	DENV-2 (predominant) followed by DENV-1
2017	DENV-2 (predominant) followed by DENV-1
2018	DENV-2 (predominant) followed by DENV-2 and DENV-1 and co-detection DENV-2 & DENV-3 and DENV-1 & DENV-3(few cases)
2019	DENV-3 (predominant) followed by co-detection of DENV-2 & DENV-3 and DENV-1 & DENV-3 (few cases)

trend (P = 0.63, τ = 0.12). Similarly, for the month of February alone (2000–2019), there were fluctuations of rainfall without any detectable trend (P = 0.31, τ = 0.17). Although, in 2019, total annual rainfall was comparable to other years in the decade, the monsoon started much earlier (18 February 2019) and continued much longer than previous years (Fig. 2). We performed Spearman's correlation coefficient test between annual rainfall and the total number of dengue cases in Bangladesh, which resulted in a poor correlation coefficient (r = 0.10). However, when we considered the sum of rainfall from January to April, the correlation coefficient increased to r = 0.39. Although only correlative, our findings indicated that early rainfall might have contributed to the increased number of dengue cases in the country. Active surveillance to monitor mosquito population abundance is absent in Bangladesh. However, previous reports indicated that *Aedes* populations peak in July and August (Ahmed et al. 2007). Therefore, in 2019, the mosquitoes had 2–3 additional months to increase the population and contribute to DENV transmission. A similar trend of increased monsoon rain and increased dengue incidence previously was observed in Southern China (Liu et al. 2020).

The third factor contributing to the size of the 2019 DENV outbreak was the failure of vector-control initiatives due to insecticide resistance. In a study conducted by researchers at the International Centre for Diarrhoeal Disease Research, Bangladesh, on *Aedes aegypti* (L.) mosquitoes found high levels of resistance against permethrin, the insecticide used by Dhaka City Corporation (Alam et al. 2018). In this study, *Aedes* were collected from seven different districts of Bangladesh during 2017–2018, including nine different locations of the capital city Dhaka, and the effectiveness of permethrin, deltamethrin, and bendocarb was tested using the CDC's bottle bioassay (Aïzoun et al. 2013). The mortality rate among *Ae. aegypti* females with permethrin ranged from 0 to 14.8% at the dose of 15 µg/bottle; doubling the dose increase the mortality rate to 5.1–44.4% after 30 min exposure. According to WHO guidelines, susceptibility to an insecticide requires the death of 98–100% of the mosquitoes at 30 min following standardized protocols, whereas if mortality <90%, populations should be considered as resistant (Collins et al. 2019). Susceptibility varied with deltamethrin (49–100%) and bendiocab (100%). After these reports were shared with Dhaka City Corporation, malathion was used as an adulticide during 2020.

Although dengue has been reported in Bangladesh since 2000, cases were mostly confined to Dhaka City until 2018. Sharmin et al. (2018) reported that 94% of DENV cases identified in Bangladesh were found in Dhaka, and Sajle et al. (2016) found that 80% of people living in Dhaka City had antibodies against DENV. Bangladesh has favorable weather to support *Aedes*-borne disease transmission throughout the year. However, the main mosquito season is associated with the monsoon period from May to August. Using district-level monthly reported dengue cases and a Bayesian inference model, Sharmin et al. (2018) estimated that 92% of annual dengue cases occurred between August and September. Therefore, meteorological forecasting to direct the timing of vector control, perhaps should begin before the 'classic' monsoon season and can help reduce the *Aedes* population and DENV burden in the country.

The mosquito control program in Bangladesh is based on the use of adulticides applied by fogging during the vector season and the spraying of larvicide (Temephos) in the drainage system for *Culex* mosquito control. The program uses a mixture of 0.5% permethrin, 0.2% tetramethrin, and up to 0.2% allethrin per liter of kerosene, which is applied through thermal fogging machines to kill adult mosquitoes. Following the dengue outbreak of 2019, Dhaka City Corporation, with the help of locally elected public representatives, began active surveillance and removal of sources of larval *Aedes* mosquitoes, including stagnant water.

In 2019, Bangladesh's insufficient preparedness and suboptimal vector-control program permitted the large DENV outbreak (Hsan et al. 2019). Outbreaks of other *Aedes*-borne virus diseases such as dengue, chikungunya, and Zika also might occur in the country in the absence of a long term plan for vector surveillance and control. The authorities should develop a centralized surveillance and data collection system to monitor the efficacy of vector-control and preventive programs. Every dengue case, whether treated in medical settings in in-patient or out-patient departments or in government or autonomous private hospitals, should be reported to the government by healthcare professionals. The local (e.g., City corporation) health department can use dynamic dashboards (patient's location at the lowest administrative level) to identity dengue-prone areas and to take immediate action accordingly. At the national level, all the Ministries of the government, including the City Corporation and the health departments should take coordinated initiatives to prevent future outbreaks.

We suggest a robust local community-level surveillance system for the timely identification of dengue cases. Each union/ward, the lowest administrative level of the country, should have a community volunteer team under the leadership of a local representative (commissioner/member/Chairman). The team will distribute leaflets containing the telephone numbers of authorities whom people with symptoms resembling dengue fever should contact. The local authority would then arrange for assessment of the medical condition of the caller/patient(s) by registered general physicians and, upon prescription from the physician, the committee would arrange testing for DENV using nonspecific protein 1 (NS-1) kit, an antigen detection kit currently used as a diagnostic tool in Bangladesh, in local diagnostic centers/hospitals. In addition, the team would collate the results of DENV diagnostic tests daily from all the diagnostic centers and hospitals within the ward/union. When a case cluster is identified (more than three cases in a 400 m radius area within three consecutive days), the team will activate mosquito control using adulticides and larval surveillance/source destruction activities (according to WHO 2009). In addition, the committee should visit the local areas monthly to eliminate *Aedes* larval habitats and raise community awareness.

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