

Seasonal Distribution and Climatic Correlates of Dengue Disease in Dhaka, Bangladesh

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Abstract. Dengue has been regularly reported in Dhaka, Bangladesh, since a large outbreak in 2000. However, to date, we have limited information on the seasonal distribution of dengue disease and how case distribution correlates with climate. Here, we analyzed dengue cases detected at a private diagnostic facility in Dhaka during 2010–2014. We calculated Pearson cross-correlation coefficients to examine the relationship between the timing of cases and both rainfall and temperature. There were 2,334 cases diagnosed during the study period with 76% over the age of 15 years. Cases were reported in every month of the study; however, 90% of cases occurred between June and November. Increases in rainfall were correlated with increases in cases 2 months later (correlation of 0.7). The large proportion of adult cases is consistent with substantial population susceptibility and suggests Dhaka remains at risk for outbreaks. Although cases occurred year-round, public health preparedness should be focused during peak months.

Dengue is caused by infection with the dengue virus (DENV), a member of the genus *Flavivirus* and is transmitted by two principal mosquito vectors of the genus *Aedes*: *Aedes aegypti* and *Aedes albopictus*.¹ It is estimated that about 400 million dengue infections occur each year in tropical and subtropical countries.^{1,2} There are four DENV serotypes, and a primary infection usually results in mild disease; however, reinfection with a different DENV serotype is more likely to result in dengue hemorrhagic fever, a more severe disease manifestation.² Dengue incidence has been associated with variations in climate. Increased rainfall supports vector habitat availability, and high temperatures promote mosquito development.³ Dengue epidemics often occur seasonally, with more cases found during wetter and warmer months. However, the complex role of local immunity patterns and population structure on transmission means that the relationship between incidence and climate remains poorly understood and often differs across settings because of local climate heterogeneity, circulating DENV serotypes, and virus–host interactions.⁴ Dengue is largely a pediatric disease in much of southeast Asia, where it has circulated for over 60 years in countries such as Thailand, Vietnam, and the Philippines.^{5–7} The epidemiology of dengue in south Asia is less clear. The first report of dengue in Bangladesh was in 1964.¹ Cases have been reported regularly in Dhaka, the capital of Bangladesh, since a large outbreak of dengue hemorrhagic fever in 2000⁸; however, limited surveillance capabilities mean that we do not know if there exists year round transmission, nor which age groups are most affected by the disease. The objective of this study was to characterize the seasonality and age distribution of dengue cases and explore the climatic drivers of transmission.

Surveillance for dengue in Bangladesh is particularly difficult as public hospitals rarely have access to diagnostic kits so diagnosis usually relies on clinician assessments, which may be affected by underreporting or misdiagnosis for other febrile illnesses.⁹ However, dengue testing is routinely performed in

the private health-care sector. Here, we analyzed data from Popular Diagnostic, one of the largest private laboratories in Dhaka.

Data consisted of de-identified dengue antibody test results, age and sex of individuals who were physician referred or self-referred for a dengue antibody test between February 2010 and December 2014. Samples were tested for dengue IgM and IgG antibodies using an immunochromatographic strip test (Bio Focus; Bio Focus Co., Ltd., Uiwang-si, Korea).¹⁰ The average cost per test was approximately US\$10. To explore the correlation between climate and dengue cases, dengue cases were aggregated by month. Meteorological data on hourly temperature (°C) and amount of rainfall (mm) were obtained from the local Meteorological Department in Dhaka. We calculated average rainfall and temperature for each month of the study period. In addition, we calculated the number of days with any rain and the mean daily minimum temperature within each month. We then calculated Pearson cross-correlation coefficients between monthly case counts and each of these climate variables. The cross-correlations were calculated using the *ccf* function in the *stats* package in R (R Foundation for Statistical Computing, Vienna, Austria). Monthly lags of up to 6 months (in both positive and negative directions) were considered. The study was approved by the institutional review board of the International Center for Diarrheal Disease Research, Bangladesh.

Of 4,439 serum specimens tested, 2,334 had evidence of IgM antibodies, suggestive of recent dengue infection. Of these cases, 1,282 (55%) were male. Cases had a mean age of 28 years and ranged from under 1 year to 91 years old (Figure 1). Individuals who tested negative for dengue had a similar mean age of 25 years. Overall, 24% (95% confidence interval [CI]: 23%, 26%) of cases were under 15 years of age (Figure 1). We observed cases throughout the year, however, cases were seasonally distributed, with peak counts observed in August and September (Figure 2A); 90% of cases occurred between June and November. Correlation between rainfall and case counts peaked at a lag of 2 months (correlation of 0.70) (Figure 2B). Peak correlation with both mean and minimum temperature was also at a lag of 2 months (peak correlation of 0.5 for mean temperature and 0.6 for minimum temperature) (Figure 2C and Supplemental Figure 1). Peak correlation with number of

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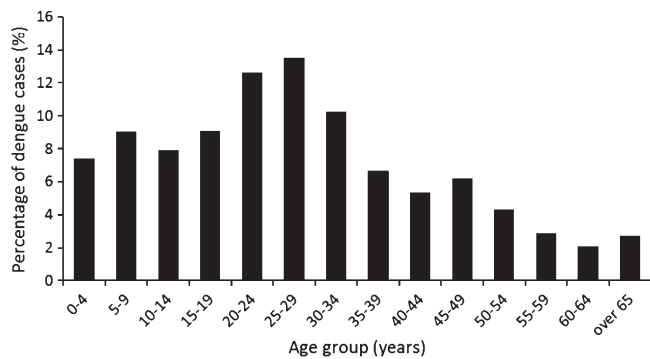


FIGURE 1. Age distribution of dengue cases for the period 2010–2014. Percentage of dengue cases in each age category over the entire study period.

days with any rain occurred at a time lag of 1 month (correlation of 0.71) (Supplemental Figure 1).

We have shown that over this 5-year period, dengue cases increased during the monsoon season each year similar to what has previously been observed from reported cases in Dhaka.⁸ We found that peak case counts occurred 2 months after peak rainfall. These findings are similar to what has been reported for rainfall and mean temperature in Vietnam (lag 1–2 months).¹¹ The seasonality of cases as well as the seasonality of rainfall and temperature were largely consistent across years (Figure 2A). Health-care providers should prepare for increased numbers of dengue cases in August and September. Given the similarity across years, we could not specifically assess whether significant changes in the timing of rainfall or temperature were associated with differences in case seasonality. However, given the potential role that temperature and rainfall have on the vector in particular, we could expect that large-scale changes in climate may change the seasonality of transmission. Despite a clear seasonal peak, cases were nevertheless observed year-round, consistent with sustained endemic transmission similar to the dengue dynamics observed in many countries in southeast Asia.^{12–14} A previous study using reported cases in Dhaka from 2000 to 2010 detected only eight cases between January and May throughout the 10-year period.⁸ The case definition used in that study relied only on physician's clinical diagnosis without diagnostic testing. Our findings highlight the importance of systematic surveillance for diagnosed cases to characterize true seasonal patterns and further suggest that physicians should consider dengue as a differential diagnosis throughout the year.

Our data were obtained from a private diagnostic facility. We cannot assume that these individuals are representative of all dengue cases in Dhaka. Health-seeking behavior is typically determined by socioeconomic status (SES), disease severity, age, and gender.¹⁵ Specifically, low-SES individuals may be less likely to afford private health-care services.¹⁵ According to a 2010 national survey on household income and expenditure, the average monthly household income was approximately US\$150.¹⁶ Therefore, many cases in Dhaka may not have been able to afford the cost (\$10) of the test and the consultancy fee at a private laboratory. Nevertheless, these differences in health-care seeking behavior are unlikely to fully explain our finding that 76% of cases are over 15 years of age. A preponderance of adult cases is consistent with only recent sustained transmission of the virus. In settings where

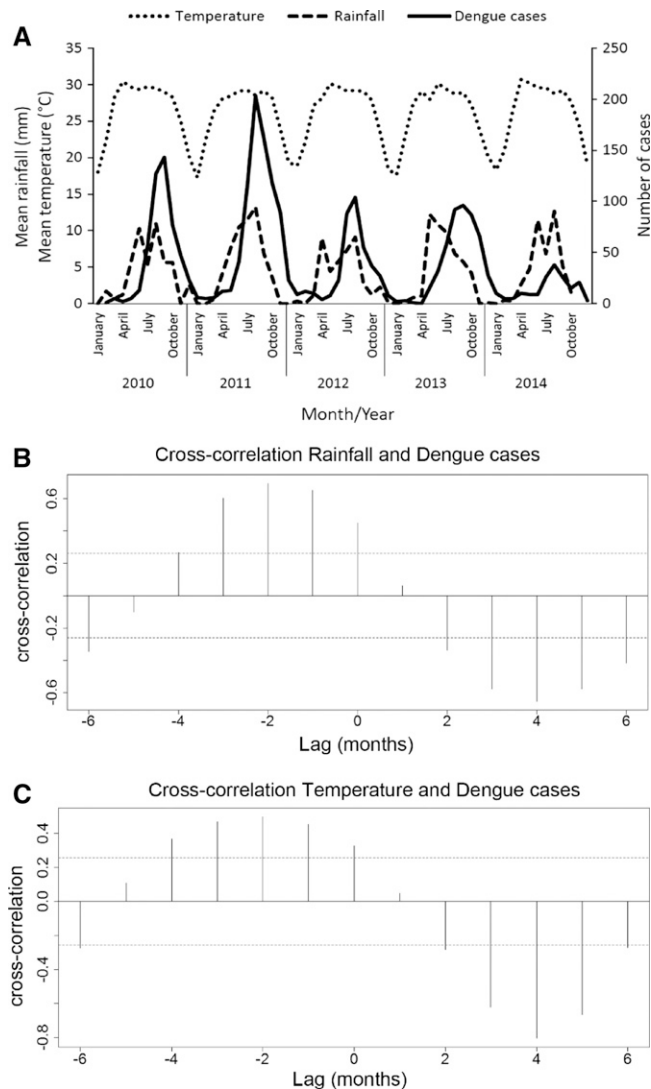


FIGURE 2. Time series and cross-correlation plots of climatic variables and dengue cases in Dhaka, from 2010 to 2014. (A) Time series of the monthly mean temperature, rainfall, and dengue cases. (B) Cross-correlation plot of monthly dengue cases and rainfall. (C) Cross-correlation plot of monthly dengue cases and temperature. The x axis gives the number of lags per month, and the y axis gives the value of the correlation coefficient between -1 and 1 . Dotted lines indicate the 95% confidence level.

the virus has circulated for long periods, most individuals are immune by the time they reach adulthood.¹⁷ For example, the proportion of dengue cases over the age of 15 years in 2010 was 52% in Thailand and only 28% in the Philippines.^{5,6} Both countries have had endemic dengue circulation for decades.¹⁸ The first observed large-scale outbreak of dengue in Bangladesh was in 2000, far later than these countries, which also supports more recent endemic transmission. A seroprevalence study in 2012 found that 80% of individuals in Dhaka had evidence of historic infection with dengue¹⁹; however, as individuals can get infected more than once, this is not a true indicator of protection from disease. If dengue continues to circulate with a high force of infection in Dhaka, we can expect an increasing number of pediatric cases.

The cases in our study represent only a tiny proportion of all dengue cases in the city. We therefore cannot use these

data to directly estimate the incidence of dengue in Dhaka. Even trends across years can be difficult to interpret due to variations in health-care seeking or changing population size and structure. However, the distribution of cases within any year is less likely to be affected by such secular trends and therefore would not impact our estimates of the seasonality of dengue and the association with climate. The sensitivity and specificity of the diagnostic assay were relatively high (sensitivity of 91.3% and specificity of 92%; www.biofocus.co.kr). Antibody cross-reactivity between dengue and other flaviviruses may occur. However, while Japanese encephalitis virus circulates in Bangladesh, it is largely restricted to rural areas.²⁰ Cross-reactivity with other flaviviruses cannot be ruled out. Delays in health-care seeking may have led to the disappearance of IgM antibodies, which peak 2 weeks after fever onset and decline over the next 2–3 months, and therefore, the presence of false negatives is possible. However, the distribution of false-positive or false-negative cases in our dataset is unlikely to differ by time of year and therefore would not impact our characterization of the seasonal distribution of dengue.

In conclusion, these findings demonstrate that transmission of dengue occurs year-round, even during cooler, drier months. Public health preparedness should nevertheless be focused during peak months to help cope with potentially large influxes of patients. Public health surveillance systems can benefit from engaging private laboratories, especially where public sector access to diagnostics is limited.

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