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Dengue outbreaks in Bangladesh: Historic epidemic patterns suggest earlier mosquito control intervention in the transmission season could reduce the monthly growth factor and extent of epidemics

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ABSTRACT

Dengue is endemic in Bangladesh and is an important cause of morbidity and mortality. Suppressing the mosquito vector activity at the optimal time annually is a practical strategy to control dengue outbreaks. The objective of this study was to estimate the monthly growth factor (GF) of dengue cases over the past 12 years as a means to identify the optimal time for a vector-control programme in Bangladesh. We reviewed the monthly cases reported by the Institute of Epidemiology, Disease Control and Research of Bangladesh during the period of January 2008–December 2019. We calculated the GF of dengue cases between successive months during this period and report means and 95% confidence intervals (CI). The median number of patients admitted to the hospital with dengue fever per year was 1554 (range: 375–101,354). The mean monthly GF of dengue cases was 1.2 (95% CI: 0.4–2.4). The monthly GF lower CI between April and July was > 1, whereas from September to November and January the upper CI was <1. The highest GF of dengue was recorded in June (mean: 2.4; 95% CI: 1.7–3.5) and lowest in October (mean: 0.43; 95% CI: 0.24–0.73). More than 81% (39/48) months between April and July for the period 2008–2019 had monthly GF > 1 compared to 20% (19/96) months between August and March of the same period. The monthly GF was significantly correlated with monthly rainfall ($r = 0.39$) and monthly mean temperature ($r = 0.30$). The growth factor of the dengue cases over the last 12 years appeared to follow a marked periodicity linked to regional rainfall patterns. The increased transmission rate during the months of April–July, a seasonally determined peak suggests the need for strengthening a range of public health interventions, including targeted vector control efforts and community education campaigns.

1. Background

Dengue is an emerging mosquito-borne flavivirus infection which is now endemic in more than 100 countries with approximately 4 billion people at risk of contracting the disease and 96 million human cases per year (WHO, 2018). Bangladesh is one of the 10 countries of the World Health Organization (WHO) Southeast Asia Region where 52% of world's total population at risk of dengue lives (WHO, 2011). Dengue fever was first recorded in the 1960s in Bangladesh (then East Pakistan) and was known as "Dacca fever" (Russell et al., 1966), but it was not until the 21st Century that it became epidemic and finally endemic with establishment of the "domesticated" mosquito vector *Aedes aegypti* and urban cycles (Dhar-Chowdhury et al., 2017; Rahman et al., 2021). Dengue is an important cause of morbidity and mortality in Bangladesh (Sharmin et al., 2015; Ahsan et al., 2021).

Managing dengue fever outbreaks in tropical countries where temperatures remain favourable for mosquito breeding and viral replication around the year is a critical challenge. Further, controlling large dengue outbreaks is expensive and involves use of insecticides to control the mosquito population and significant resources to manage sick patients at hospitals. Current vector-control in Bangladesh is a mandate of the local government – the City Corporation/Municipality is responsible for controlling mosquito populations. The programme is largely based on spraying insecticidal chemicals which aim to kill adult mosquitoes,

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especially during the peak dengue period (August–September) when usually a large number of dengue cases are detected in hospitals (Al-Amin et al., 2020). Detecting the critical control points is central to managing dengue. One of these points of intervention involves suppressing the mosquito vector activity at the optimal time in annual population fluctuations, in order to achieve the lowest biting population when environmental conditions for emergence and transmission are most favourable.

Dengue virus is transmitted between humans and mosquitoes: *Ae. aegypti* and *Ae. albopictus* are the principal vectors of the disease, and both mosquito species are widely distributed in Bangladesh (Rahman et al., 2021). In 2019 the country experienced one of the largest dengue fever outbreaks in the history of the country (Ahsan et al., 2021). More than 100,354 people being hospitalized and 266 people (0.1% of hospitalized cases) dying between 1st January 2019 and 31st December 2019 (Ahsan et al., 2021). Case data are regularly updated by the Directorate General of Health Services (DGHS, 2019) and monthly updates are publicly shared by DGHS's surveillance and research wing, Institute of Epidemiology, Disease Control and Research (IEDCR) (IEDCR, 2019). Approximately 90% of the cases are reported in the capital city, Dhaka, consistent with spatial models predicting 94% cases to be localized in Dhaka (Sharmin et al., 2018). An observational study reported 90% of observed cases between June and November during 2010–2014 (Salje et al., 2016), whilst a model predicted more than 92% cases between August and September in 2000–2009 (Sharmin et al., 2018).

We analysed the monthly reported dengue cases recorded between January 1st 2008 and December 31st 2019 to estimate the monthly growth factor (GF) in cases to describe seasonality and the mean peak infectious period in Bangladesh. Finally, we compared the monthly GF with monthly rainfall and temperatures recorded in the capital city Dhaka for the period of 2008–2019.

2. Materials and methods

DGHS maintains national surveillance records of hospitalized patients with dengue and chikungunya fever and these records are updated weekly or occasionally daily (DGHS, 2019). The monthly reports shared by the Institute of Epidemiology Disease Control and Research (IEDCR) include the dengue cases admitted in 14 government and 35 private hospitals located in the capital city, Dhaka and 523 private and government hospitals outside Dhaka (IEDCR, 2019). A person is admitted as a dengue patient based on: clinical diagnosis with signs and symptoms for suspected dengue cases including fever, rash; and/or laboratory tests for dengue virus (immunoglobulin (IgM or IgG), non-structural protein 1 (NS1) of dengue virus; or simply by complete blood count, haematocrit and platelet counts) (DGHS, 2019; IEDCR, 2019). We used the monthly dengue cases reported from January 2008 to November 2019 (IEDCR, 2019).

We estimated the monthly growth factor (GF) of dengue cases by dividing the number of dengue cases detected in a given month by the number of dengue cases of the previous month, and the procedure was repeated for each month of the period 2008–2019. That is, $GF_t = \frac{Month_{t+1}+1}{Month_t+1}$, where subscript "$t$" indicates the current month.

We added 1 to the number of cases for all the months to overcome the occurrence of zeroes in some months. The distribution of the GF was skewed, and it was log-transformed prior to further analysis. A linear model was used to evaluate the differences in log(GF) between months (Supplementary Fig. S2). The estimated log(GF) and its 95% confidence interval (CI) was then back-transformed (by using exponential values) to the original scale for ease of interpretation. The GF of 2.42 for the month of June is interpreted as meaning there would be 2.42 times more cases in the month of July. We collected meteorological data (hourly temperature and daily total rainfall) for the period of 2008–2019 from the Bangladesh Meteorological Department. We calculated the Pearson's correlation coefficient between monthly log(GF) with monthly rainfall and temperature (°C), and between monthly log(GF) and rainfall or temperature in the previous month or 2-month time for the period of 2008–2019. We also calculated correlations between monthly reported log (no. of cases +1) and monthly rainfall and monthly temperature.

3. Results

The median number of patients per year admitted to the hospital because of dengue fever was 1566 (interquantile range, IQR: 611–3899). The highest number of patients were hospitalized in the month of August, with a median of 409 patients (IQR: 168–936) and lowest in the month of March, with a median of 2 (IQR: 0–17) patients (Fig. 1). During the study period, the overall mean GF from month to month was 1.2 (95% CI: 0.45–2.43). However, only in 4 months (April–July) was the monthly GF significantly >1 while in 4 months (September–November and January) this value was <1 with 95% confidence intervals excluding 1 (Fig. 2 and Supplementary Table S1). More than 81% (39/48) of months between April and July for the period 2008–2019 had mean monthly GF > 1 compared to 20% (19/96) months between August and March of the same period (Fig. 3). June showed the highest GF with a mean value of 2.42 (95% CI: 1.67–3.53) while October had the lowest value with a mean of 0.45 (95% CI: 0.25–0.74) (Fig. 2 and Supplementary Table S1).

The correlation coefficient between monthly GF and rainfall was 0.39 (95% CI: 0.24–0.52, $n = 141$, $P < 0.0001$) with lower values for one- or two-month lag periods (Supplementary Table S2). The correlation coefficient between monthly GF and monthly mean temperature (°C) was 0.30 (95% CI: 0.15–0.45, $n = 141$, $P = 0.0002$), again with lower values for one- and two-month lag periods (Supplementary Table S2). The correlation coefficient between monthly reported log-converted dengue cases and rainfall was 0.33 (95% CI: 0.17–0.46, $n = 141$, $P < 0.0001$) rising to 0.55 (95% CI: 0.42–0.65, $n = 140$, $P < 0.0001$) for a month lag period and 0.60 (95% CI: 0.48–0.69, $n = 139$, $P < 0.0001$) for a two-month lag period. For temperature, the correlation coefficient with monthly reported log-converted cases was 0.31 (95% CI: 0.15–0.45, $n = 141$, $P = 0.0001$) rising to 0.49 (95% CI: 0.36–0.61, $n = 140$, $P < 0.001$) for a month lag period and 0.55 (95% CI: 0.43–0.66, $n = 139$, $P < 0.0001$) for a 2-month lag period temperature (Supplementary Table S2).

4. Discussion

Despite vector control efforts over the past decade, through targeting of mosquitoes and of their breeding sites, dengue continues to be an important public health challenge in Bangladesh. More than 81% of the months of April, May, June and July of the period 2008–2019 had a monthly GF of >1 compared to 20% months of the rest of the months (August to March) of the same 12-year period. These consistent findings over a significant period suggests importance of early vector control programme in Bangladesh.

We detected the highest GF in the month of June indicating the peak transmission month, i.e. for each dengue case the highest number of secondary cases generated in the month of June. This might be because of a combination of favourable environmental factors (rainfall which is coincident with higher temperatures) and availability of susceptible human hosts at the beginning of the transmission seasons. June is the first official month of monsoon in Bangladesh and one of the warmest months of the year in the country (Supplementary Fig. S1). The combination of higher rainfall creating favourable breeding sites for *Aedes* mosquitoes and higher temperatures, which are likely to shorten the extrinsic incubation period and biting interval, are expected to result in a more rapid transmission cycles and infection rates (Haider et al., 2017). We propose it would be optimal to start the vector-control programme from April because the estimated GF started to exceed 1 from April and GF remained above 1 up until July (Supplementary Table S1). Our analysis showed that dengue cases are increasing at a higher rate during the early

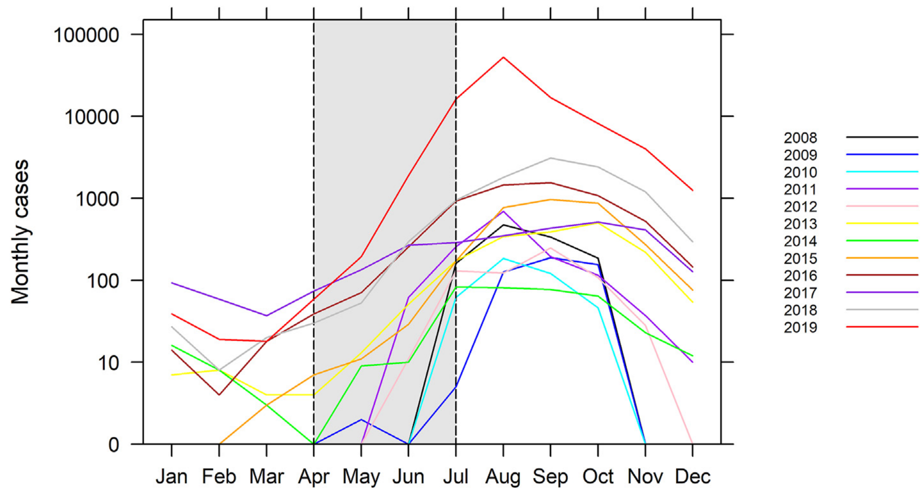

Fig. 1 Number of dengue cases reported through national dengue fever surveillance in Bangladesh, 2008–2019.

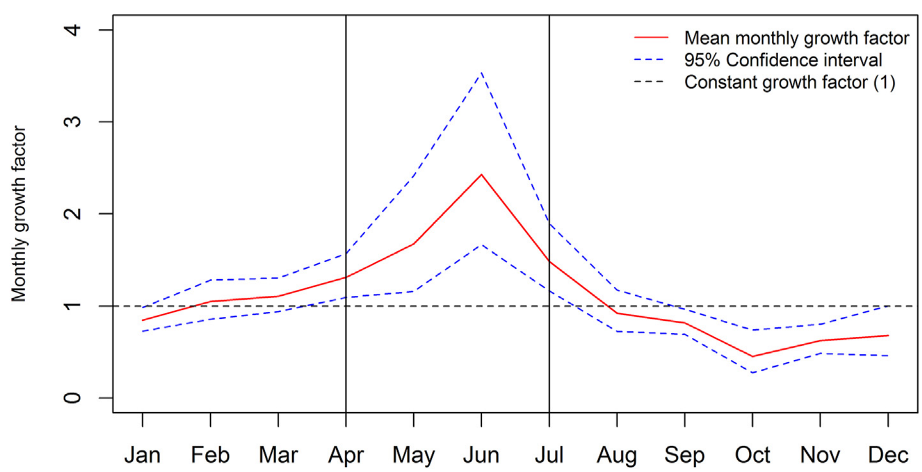

Fig. 2 The monthly growth factor (GF) of dengue cases in Bangladesh (2008–2019). The peak growth factor was observed in the months of June with a mean value of 2.4, indicating that the number of cases would be 2.4 times higher in the month of July. The lower value of 95% CI of the GF for the months April–July is > 1 indicating a high transmission period. The period between two vertical lines indicates the GF > 1.

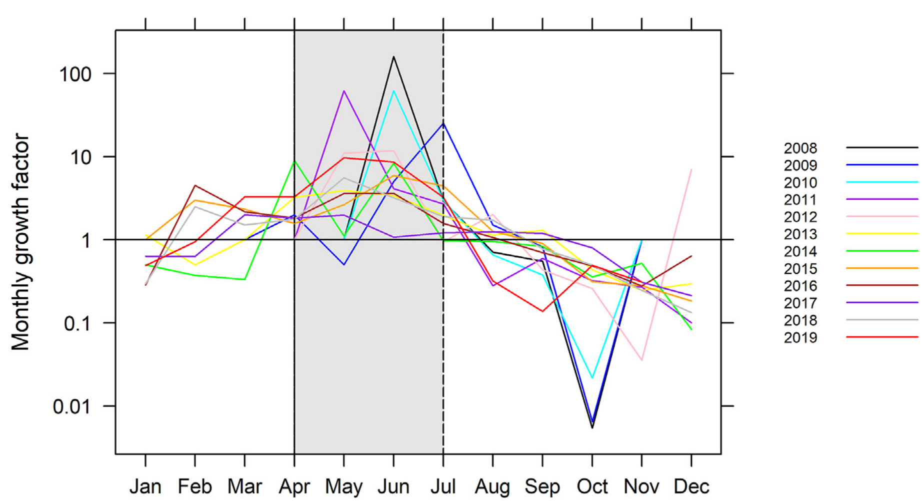

Fig. 3 The monthly growth factor (GF) of dengue cases in Bangladesh (2008–2019). More than 81% (39/48) months between April and July of the period 2008–2019 had monthly GF > 1 compared to 20% (19/96) of the months between August and March of the same period.

transmission season (April–July) and thus starting the vector control programme earlier could help in controlling the dengue incidence more effectively. We recommend piloting earlier community engagement for destruction of *Aedes* breeding habitats which may influence the overall control positively and potentially reduce case incidence (Liu et al., 2018).

A previous study reported that most dengue fever cases (> 90%) are recorded between August and September (Sharmin et al., 2018). This is also the peak of adult *Aedes* mosquito activity period in Bangladesh (Ahmed et al., 2007). Our estimation also recorded a high correlation between the monthly rainfall and mean temperature with the monthly GF. This indicates that the impact of rainfall and temperature is delayed roughly by a month. This is due to the fact that the monthly GF of a particular month is an outcome of dengue cases occurring in the previous months. This is further evident from the correlation coefficient of monthly reported dengue cases which shows a better correlation with the one- or two-monthly lag temperature and rainfall. Therefore, our analysis suggests the importance of targeting the vector control period earlier in the dengue transmission season (for example, starting from April), i.e. when the GF is > 1, and this application of control measures might be more effective in suppressing later emergence and spread.

During the early transmission period, a larger proportion of the human population is expected to be naïve and susceptible to dengue virus infection, which is likely to explain, at least in part, why the rate of transmission increases rapidly. In addition to organised control measures with careful timing for application as suggested by this study, it is recommended that people take precautions against mosquito bites in order to further limit the size of the outbreak.

This study has some limitations. The reported dengue cases were recorded from hospital admitted patients only, whereas dengue is usually a self-limiting infection in most primary infections (WHO, 2009). Furthermore, most dengue cases are asymptomatic which are not recognized in a syndromic surveillance system. More than 50% dengue cases were reported as asymptomatic (symptomatic to inapparent) in a study in Thai school children (Endy et al., 2011) whereas in Costa Rica 36% (Iturrino-Monge et al., 2006), in Pakistan 25% (Mohsin et al., 2016) and in Cambodia 7.5% (Ly et al., 2019) of dengue cases were reported as asymptomatic. WHO recognizes this problem and a modelling study suggesting that out of a total of 390 million dengue virus infections per year perhaps only 96 million manifest clinical signs (Bhatt et al., 2013; WHO, 2018). However, although asymptomatic cases are likely a larger proportion of total dengue cases this is impractical to monitor. Reporting of symptomatic cases is the only practical and feasible sentinel without a randomised regular sensitive screening diagnostic programme. Data are also recorded only from selected hospitals: for example, during 2019, a total of 51,810 cases were admitted in different hospitals in Dhaka city whereas 49,544 cases were recorded from rest of the country. Thus, our analysis reflects the scenario of Dhaka rather than whole country. However, previous studies, including spatial modelling, have shown that more than 90% of the dengue cases admitted to the hospital are recorded in Dhaka city (Sharmin et al., 2018). Thus, the overall trend and the change rate are relevant for dengue fever epidemiology and disease control in Bangladesh.

5. Conclusions

The growth factor of the dengue cases over the last 12 years appeared to follow a marked periodicity linked to regional rainfall patterns and is coincidental with higher environmental temperatures. The increased transmission rate during the months of April–July, a seasonally determined peak, indicates for a potential opportunity to strengthen a range of public health interventions. Currently, July–September is considered as the dengue outbreak period in Bangladesh and thus resources are allocated to control the vector mosquitoes more intensively during this period of the year. These data showed that dengue cases are consistently increasing at a much higher rate during April–July compared to the rest of the months examined and thus piloting a vector control programme that starts earlier in the season, might be more efficient in limiting the dengue outbreaks in Bangladesh.

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Ethical approval

No individual-level data were used in this manuscript, and thus the study does not require any ethical approval.

CRediT author statement

Najmul Haider: conceptualization, methodology, data analysis, visualization, writing - original draft. Yu-Mei Chang: data analysis, visualization and validation, writing - review & editing. Mahbubur Rahman: data curation, writing - review & editing. Alimuddin Zumla: supervision, writing - review & editing, fund acquisition, validation. Richard Kock: methodology, supervision, writing-review & editing, fund acquisition.

Data availability

All the data used in this article are publicly available at: https://old.iedcr.gov.bd/website/index.php/surveillance/219. The summary analyses are presented as figures and tables in this article. More details about the data or the analysis are available from corresponding author upon request.

Declaration of competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.crpvbd.2021.100063.

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