**Title: Two Decades of Dengue Outbreaks in Bangladesh (2000-2022): Climate Change, Seasonality, and future control plan**

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**Background:** The dengue virus has reappeared in Bangladesh in 2000 and the virus has been detected every year since then. The objectives of this study are to summarize the monthly incidence of dengue infection for the period 2000-2022 for Bangladesh, to understand the seasonality and trend, and to quantify the impact of climatic factors.

**Methods:** We have performed exploratory statistical analyses, two nonparametric tests: Mann-Kendall and Sen’s slop test for trend and variation, and fitted a time series Poisson regression model to identify the impact of meteorological factors on the incidence of dengue cases, their seasonality, and trend. Finally, we have forecasted dengue cases using an autoregressive integrated moving average (ARIMA) model for the next 12 years.

**Results:** Between 2000 and 2022, a total of 244,246 dengue cases were reported with 792 fatal outcomes indicating an overall case-fatality ratio of 0.32%. Compared to the first decade (2000-2010) the annual dengue cases have increased by eight times, and annual deaths have increased around 2 times in the recent decade (2011-2022). The mean monthly cases reached a peak in August with the monthly growth factor remaining above one significantly during April-July. We found an increasing trend of dengue cases in Bangladesh with a much stiffer rise after 2018. Monthly mean temperature (Incidence risk ratio [IRR]: 1.26 (95% CI: 1.25-1.27), first-lagged rainfall (IRR: 1.08 (95% CI: 1.07-1.09), and second-lagged rainfall (IRR: 1.17 (95% CI: 1.16-1. 18) were found to be significantly associated with monthly dengue incidence in Bangladesh.

**Conclusion:** Over two decades, Bangladesh has experienced a significant burden of dengue cases with regular outbreaks. The increased local temperature and unusual rainfall might have contributed to this increased incidence of dengue cases in Bangladesh.

**Word count: 3,334**

**Introduction:**

Dengue fever is caused by four distinct serotypes of the dengue virus (DENV:1-4) of the Flaviviridae family [1]. DENV is transmitted to humans primarily by two species of Aedes mosquito: *Ae. aegypti* and *Ae. albopictus* [1,2]. Most infections (>80%) are self-limiting with no or mild clinical manifestation resulting lifelong immunity for the serotype [3]. However, infections with different serotypes, known as secondary dengue infection, may result in severe dengue with a higher case-fatality ratio[4]. Dengue infection is currently a major global health concern, with an estimated 390 million dengue infections per year, including 96 million clinical cases [5,6]. South and Southeast Asia is considered to be the hotspot of dengue infection with more than 50% of cases recorded in the regions [7].

The first dengue outbreak in Bangladesh was reported in 1964 (formerly, East Pakistan), and the term "Dacca fever" was coined. After that, there has been a long period of no report of a dengue outbreak in the country. The first official dengue outbreak in Bangladesh was reported in 2000, and since then, dengue has become endemic in the country, posing a significant health challenge [8]. The country has witnessed a significant increase in dengue incidence in recent years, with an estimated 40 million people being infected nationally and 2.4 million annual infections [9]. However, the reported number seems to be only a fraction of the total infected cases [10,11]. The largest dengue outbreak in Bangladesh occurred in 2019, with over 101,000 cases and 164 deaths reported [10,11]. In 2020, the number of cases dramatically decreased to 1,405 with only three confirmed deaths possibly a consequence of lockdown-related measures during the first year of the COVID-19 pandemic [11,12]. In 2021, there was a sharp increase in dengue cases again, with over 28,000 cases and 105 reported deaths [13,14]. In 2022, Bangladesh reported the highest number of dengue-related deaths (266) in the country [15]. The 2022 outbreak is characterized by the late onset of the outbreaks with the highest ever reported deaths, partly attributed to the occurrence of a new serotype (DENV-4) in the country [11].

Over the past few years, number of dengue cases has been steadily increasing with significant variations in seasonal and regional patterns. Analysis of data from 2000 to 2017 revealed that almost half of the dengue cases occurred during the monsoon season (May-August) and the post-monsoon season (September-December) [16]. However, a shift in seasonal patterns has been observed since 2014, with dengue cases being reported during the pre-monsoon season as well [16]. During 2015-2017, the number of dengue cases during the pre-monsoon season was more than seven times higher compared to the previous 14 years [16].

Climate change including changes in precipitation, humidity, and temperature, as well as rapid unplanned urbanization, were identified as strong predictors of an ecological imbalance that has led to an increase in dengue cases in Bangladesh [16]. This suggests that the dengue transmission season could eventually extend year-round, with a higher chance of outbreaks occurring at any time. In this study, we aim to i) summarize the annual and monthly cases for the past 22 years by comparing the incidence of cases in the first [2000-2010] and recent decade [2011-2022], ii) identify the trend and seasonality of dengue cases, and iii) quantify the impact of climatic factors for the monthly incidence of dengue cases in the country. Identifying trends and seasonality in dengue cases can aid health authorities and other government departments in effectively allocating resources to control the spread of the disease.

**Methods:**

**Data sources**

The data on the number of reported dengue‐infected people have been extracted from the Directorate General of Health Services (DGHS)'s website from January 2000 to December 2022 [15]. We used the definition of dengue cases used by the Ministry of Health and Family Welfare, Bangladesh, which was discussed in our earlier article [10]. We collected three-hourly temperature and daily rainfall data from Bangladesh Meteorological Department (BMD) over the period 2000–2022 [17].

**Variables**

In this study, the monthly number of dengue cases are used as the main outcome variable. Two climatic variables- temperature and rainfall are used as the covariates for the regression analysis. In addition, two lagged variables rainfall in lag 1 and lag 2 have also been used as the predictors for the analysis to capture the actual impact of those meteorological elements.

**Statistical analysis**

We performed the analysis of the dengue incidence and meteorological data for the period of 2000-2022. In the first stage, descriptive analysis is conducted to determine the characteristics of confirmed dengue cases and deaths, and showed the mean, minimum, maximum and standard deviation in each year and in each month for the entire period. Then we have performed a comparison of dengue cases, deaths, and weather parameters in two decades (2000-2010 and 2011-2022) using paired sample t-test. In the third stage, we have calculated the monthly growth factor (GF) of dengue cases dividing the number of dengue cases reported in a given month by the number of dengue cases reported in the previous month and repeating this process for each month from 2000 to 2022 [18]. Therefore, the formula for the growth factor can be given by

where indicates the number of dengue cases in th month. To avoid the occurrence of zeros in some months, we added 1 to the total number of cases for each month. This allows us to obtain a real-valued measurement of the GF for the above equation. The distribution of GF is skewed, therefore, we have used first natural log-transformation before the data being further examined. However, we have also performed a reverse transformation of the log (GF) values by exponentiating values to convert them to the original scale for the ease of interpretation[19].

We have then used a time series count generalized linear model (GLM), more specifically, a time-series Poisson regression model to determine whether the climatic factors are associated with the dengue cases over time. The non-normality, heteroscedasticity, and non-linearity that characterize count data can be fitted easily using GLMs. The GLMs are implemented by selecting an appropriate link function and the distribution for data. Models for count time series need to be handled and fitted carefully as the observations may possess auto correlation and they are nonnegative integers [20]. As mentioned, we have applied a count time series GLM model employing the Poisson distribution with a log link function in this research as it is one of the most appropriate models and offers a parsimonious way to fit time series count data [21, 22].

Finally, we have performed forecasting using the autoregressive integrated moving average (ARIMA) model. The ARIMA model is a data-driven, exploratory strategy that enables us to fit a suitable model and forecast values. By removing high-frequency noise from the data, the model discovers local patterns by assuming that the time series values are linearly related. We also conducted a Mann-Kendall (M-K) trend analysis to determine whether any trends exist and whether they were going in an upward or downward direction. As a nonparametric test, the M-K approach can determine whether a trend is monotonous and whether it is positive or negative. We also performed the Sen's slope test to assess variations in annual dengue cases and deaths.

Dengue cases were utilized as the outcome variable in this model, along with data from the Bangladesh Meteorological Department (BMD) on temperature and rainfall. To capture the actual impact of rainfall on dengue incidence across time, we additionally employed two lagged variables of meteorological elements, mainly rainfall in lag 1 and 2. After eliminating predictors with a higher multicollinear relationship, we have arrived at average temperature, rainfall (in lag 1), and rainfall (in lag 2) as the final set of predictors for the monthly dengue incidence in Bangladesh. These various methods have assisted us in reaching a tenable conclusion regarding the trend of dengue incidence and the possible meteorological factors influencing dengue cases in Bangladesh. We have used statistical program R, version 3.5.2.2 for the analyses.

**Results:**

Between 2000 and 2022, Bangladesh reported a total of 244,246 dengue cases with 792 fatal outcomes (case-fatality ratio: 0.32%). Of the 244,246 cases, 101,354 (41%) were recorded in the year 2019 alone. Of the 792 deaths, 281 (35%) were recorded in the year 2022. The mean annual number of dengue cases detected in Bangladesh was 10,619 (standard deviation [SD]=23,971). The highest number of annual cases was reported in the year 2019 with 101,354 and the highest number of deaths was recorded in 2022 with 281 deaths, which is 35% of total death recorded in the past 23 years in Bangladesh **(Fig 1)**. Most of the dengue-related deaths were recorded after 2018, with more than 69% (n=550) deaths recorded during this time. Out of the 23 years, no deaths were recorded in 10 years **(Fig 1)**.



**Fig 1: Top: Number of dengue cases and deaths over the period 2000-2022. Bottom: Number of monthly dengue cases and deaths.**

In the first decade of this century (2000 to 2010), the mean annual number of dengue cases was 2,216 (±2,123) which has increased over eight times in the recent decade (2011-2022) at 18,321 (±31,778) **(Table 1)**. Between these two periods, the mean number of annual deaths due to dengue infection has increased by 2.2 times (21.18 cases vs 46.58 cases). The highest average number of cases was recorded in August (3407 cases) and the lowest in February (7.3 cases) **(Fig 1)**.

The average annual temperature was 26.35 °C (SD=3.72) during the first decade (2000-2010) and 26.84 °C (SD=3.76) during the recent decade (2011-2022) (**Table 1**). The annual rainfall had decreased by 314 mm between two decades (2078.66 mm vs. 1764.50 mm) (**Table 1**).

**Table 1: Comparison of dengue cases, deaths, and weather parameters between the first (2000-20210) and the recent decade (2011-2022) in Bangladesh**

|  |  |  |  |
| --- | --- | --- | --- |
|  | First decade (2000-2010) | Recent decade (2011-2022) | p-value |
| Mean annual dengue cases (SD) | 2216.64 (2123.62) | 18321.92 (31778.90) | 0.219 |
| Mean annual dengue deaths (SD) | 21.18 (30.69) | 46.58 (90.90) | 0.853 |
| Mean temperature °C (SD) | 26.35(0.49) | 26.84 (0.37) | <0.001 |
| Mean annual rainfall (SD) | 2078.66 (459.68) | 1764.50 (448.32) | 0.188 |

The overall mean GF from month to month was 1.37 (SD=0.86). However, in four months (April-July), the monthly GF was above one (lower 95% confidence interval >1), while in the rest of the months, the monthly GF was less than 1 (95% confidence interval crossed 1). More than 77% (71/92) of months between April and July for the period 2000–2022 had mean monthly GF > 1 compared to only 16% (30/184) of months between August and March of the same period. The month of June had the highest GF with a mean value of 3.47 indicating that cases would be three times higher in the next month (July). The lowest GF was recorded in December with a mean of 0.54 (95% CI: 0.40 to 0.69) indicating that cases in January would be halved compared to the number of cases recorded in December (**Fig. 2**).



**Fig 2: Top:** Mean monthly growth factor for the period of 2000-2022. Bottom: The Monthly growth factor for the individual year 2000-2022. The dotted horizontal line indicates monthly growth factor 1 (same number of cases in two subsequent months).

**Table 2: The Mann-Kendell trend test of dengue cases in Bangladesh**

|  |  |  |
| --- | --- | --- |
| **Test** |  | |
| ***Mann-Kendell trend analysis*** | **Tau** | **p-value** |
|  | 0.26 | 0.139 |
| *Sen’s Slop test* |  |  |
|  | Sen’s Slope | 95% Confidence Interval |
|  | 171.67 | -46 to 687 |

In the GLM, the estimated effect of each variable is presented as the incidence risk ratio (IRR). The results suggest that dengue cases would rise by 26% for an increase of one-degree centigrade (°C) temperature. For each additional centimeter (cm) of rainfall in the first lagged month, the number of dengue cases increased by 8% (IRR= 1.08 [95% CI: 1.07-1.09]), and in the second lagged month increase the cases by 17% [IRR=1. 17 (95% CI: 1. 16 -1.18)] **(Table 3)**.

**Table 3: The incidence risk ratio (IRR) of average temperature and rainfall to Dengue cases in Bangladesh using time-series count Generalized Linear Model.**

|  |  |  |
| --- | --- | --- |
|  | IRR (95% CI) | P-value |
| Average temperature | 1.26 (1.258 – 1.265) | <0.001 |
| Rainfall (lag 1) in centimeter | 1.08 (1.079 – 1.086) | <0.001 |
| Rainfall (lag 2) in centimeter | 1.17 (1.168 – 1.175)) | <0.001 |

In the M-K trend analysis, we found a positive trend of reported dengue cases (p <0.001 and tau = 0.26). In Sen’s slope test, the slope was 171.67 (95% CI: -46 to 687) indicating an upward trend in upcoming months (**Table 2 and Fig 3**). In the ARIMA model, we detected an increasing trend for the first few years then started to decline. However, a stiff rising of cases is observed after 2018 except for 2020 (the first year of the Covid-19 pandemic).

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Description automatically generated

**Fig 3: Observed and forecasted number of dengue cases in Bangladesh using Autoregressive moving average (ARIMA) model including 95% confidence interval**

**Discussions:**

Dengue fever became an important public health challenge for Bangladesh. The number of cases has increased eight times and deaths by almost 2 times between the first and second decade of this century. Between these decades, the annual temperature increased by 0.49 °C, and annual rainfall decreased by 314 mm. Although the amount of annual rainfall had decreased, the rainy season has changed significantly with unusually early or late rainfall outside the typical monsoon season in Bangladesh (July-October) [20]. Rainfall facilitates mosquito breeding and thus the number of dengue cases increases significantly. The monthly growth factor remains above one significantly for four months (April to July) which overlaps the hot and humid period of the year.

Two large dengue outbreaks occurred in Bangladesh in the year 2019 and 2022 both characterized by unusual weather patterns and the occurrence of two different serotypes. The 2019 outbreak was characterized by early rainfall and the introduction of a new serotype of DENV-3 in the country [10]. The 2022 outbreak was characterized by the late onset of rainfall and prolongation of monsoon along with the introduction of a new serotype, DENV-4 in the country [21]. The occurrence of a new serotype exposed a large naïve population in a densely populated country like Bangladesh. A large proportion of the population is already infected with one of the serotypes of DENV with more than 80% of people living in Dhaka having antibodies against DENV [22]. Thus, any subsequent infections raise the risk of developing severe dengue through antibody-dependent enhancement (ADE) [4]. The deaths of many people in the year 2022 when the new serotype DENV-4 was introduced were probably associated with secondary dengue infection.

Bangladesh’s dengue season is characterized by hot humid periods running between June to August. This is the period with the highest amount of rainfall in the country facilitating Aedes mosquito breeding in the country[11]. The monthly mean growth factor above 1 for April – June for 22 years indicates that for dengue cases for each subsequent month, the cases will surpass the number of cases of the current month. However, the highest number of cases are reported in the month of August, one of the warm and humid months in the country. Our analysis showed monthly mean temperature (26%) and both the first and the second lagged month’s rainfall (8% and 17%, respectively) a significant increase in the incidence of dengue cases. These findings are consistent with an earlier study in Bangladesh that showed that peak dengue cases occurred two months after the peak rainfall [22]. Similar findings were reported in Vietnam with the dengue incidence being associated with both first and second-lagged months[23]. These findings are biologically plausible as rainfall allows approximately two generations of dengue cases over a month or four generations over two months period. A generation interval is a time difference between a primary human infection and a second human infection originating from the first human case through two bites the mosquitoes[24]. To accomplish a generation interval the virus and mosquito undergo several phases including intrinsic incubation period in humans, human-mosquito transmission (first bite), extrinsic incubation period in mosquitoes, blood meal digestion period, and finally mosquitoes-to-human transmission (2nd bite)[24]. Ideally, for the dengue virus, the generation interval completes at around 16 days at 28-32 °C [24].

Globally and regionally in South and Southeast Asia, dengue cases are increasing. DENV infection increased by more than 46% between 2015 and 2019 in the region [7]. We found an increasing trend in the reported number of dengue cases in Bangladesh. This increasing trend was much stiffer after the serotype DENV-3 was introduced in the country in 2018 [12]. This increased trend is possibly linked with climate change in the region attributed to increased temperature and unusual rainfall, urbanization, population growth, inadequate water supply and storage practice, poor sewer, and waste management system, rise in global commerce and tourism [7].

The case fatality ratio (CFR) of primary dengue infection is very low with an estimation of 0.018% - 0.1% [25]. However, the CFR of secondary dengue infection is high, although precise estimates are not available, some studies show more than 1% and reaching up to 4% [26]. Bangladesh’s overall CFR of dengue infection (0.32%) seems slightly higher considering the CFR reported in other South and Southeast Asian countries [7]. However, it needs to be kept in mind that more than 93% of dengue-related deaths in Bangladesh were recorded after the introduction of the serotype DENV-3 in 2019. Thus, secondary infection is likely contributing to higher dengue-related deaths in Bangladesh. In addition, the CFR of the dengue virus infection might have been affected by a lack of active surveillance and missing the mild and asymptomatic cases, and not recording the cases outside the public hospital and few selected private hospitals in Bangladesh or weaker health care system in the country[12]. In some years, the CFR was very high for example, in the year 2003, the CFR was 2.1 (total cases 486), in the year 2000, 1.68 (total cases 5,551), and in 2022, 0.45 (total cases 62,382).

Controlling vector-borne diseases in tropical countries where temperatures, humidity, and rainfall remain favorable for breeding mosquitoes during most periods of the year is a difficult task[11]. Researchers raised concern over the development of insecticide resistance [11], and the failure of developing a successful dengue vaccine[27]. The prospect of *Wolbachia-*related intervention is still far from applying to field settings. In this situation, an integrated and holistic vector management plan while engaging the local communities is key for controlling Aedes-borne diseases, especially in resource-limited countries. Regular destruction of mosquito breeding habitats and increasing surveillance for detecting active cases should prioritize in controlling dengue virus infection in Bangladesh. Policymakers need to design an Aedes-borne disease management plan by considering a range of diseases that Aedes mosquito can transmit including Chikungunya, yellow fever, zika virus, West Nile, Japanese Encephalitis, Eastern Equine Encephalitis, Ross River, Rift Valley fever, and the LaCrosse virus[11].

We argue to interpret and generalize our findings with caution. We relied on the reported number of cases from the Ministry of Health and Family Welfare. This number seems to be an underestimation of actual cases. A modelling study based on the national seroprevalence of DENV antibodies predicted an annual infection of 2.4 million cases with 40 million cases nationwide [28]. However, dengue infection is underestimated globally as this is difficult to diagnose asymptomatic or mild cases that never reach hospital settings. Although mild cases are missed more frequently, the severe cases would likely visit the hospital and thus be counted as numerators in our estimation. Thus, our estimation did not overlook the worst-case scenario.

**Conclusion:**

Between the first (2000-2010) and the second decade (2011-2022), dengue cases have increased by 8.3 times, and annual deaths have increased by 2.2 times in Bangladesh. This growth of cases is partly explained by the influence of global warming with an increase of 0.49°C annual temperature as well as changes in duration and length of the rainy season. Unusual rain including early rain or late rain in the monsoon season likely contributed to extending the length of the dengue transmission season in Bangladesh. The monthly total rainfall of the first-lagged month and second-lagged rainfall showed a greater influence on monthly dengue incidence in Bangladesh. Controlling dengue virus infection requires an integrated and holistic vector management plan while engaging the local communities. Regular destruction of mosquito breeding sites and increasing surveillance for detecting active cases are key in controlling dengue virus infection.

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**Author contribution statement:** NH originally planned the study, MNH and IK collected the data, NH, MNH and MA analyzed the data. NH, IK and MNH prepared the first draft manuscript and MABC, MR, MA, MB, MJU, RG, IR, and AZ reviewed the draft manuscripts. All authors approved the submission of the manuscript.

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**Ethics statement:** This study does not include any individual-level data and thus does not require any ethical approval.

**Data availability statement:** All the dengue data presented in this manuscript are publicly available on Bangladesh’s Ministry of Health and Family Welfare’s Directorate General of Health Services website (<https://dghs.gov.bd/> ). The meteorological data were purchased from Bangladesh Meteorological Department and are restricted to use for research purposes only and anyone interested in these data can request Bangladesh Meteorological Department (<https://live3.bmd.gov.bd/> ).

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