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

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**Abstract: (Target: 300 words, current count: 312 words)**

**Background:** After 1964, the dengue virus reappeared in Bangladesh in 2000 and then the virus is detected every year. The objective of this study was to summarize the annual dengue cases for the period 2000-2022 and perform a time series model to identify whether annual cases and deaths have any increasing or decreasing trend.

**Methods:** We collected monthly reported dengue cases and deaths data from the Ministry’s Health website and meteorological data from the Bangladesh Meteorological Department for the period of 2000-2022. We performed time series count Generalized Linear Model (GLM), M-K trend test, Sen’s slop test, and times series forecasting autoregressive integrated moving average (ARIMA) model to detect the impact of meteorological parameters on the incidence of dengue cases, seasonality, and trend of dengue cases.

**Results:** Between 2000 and 2022, Bangladesh's overall annual mean (SD) dengue cases was 10619 (±23972). Compared to the first decade (2000-2010) the annual dengue cases have increased by 8.3 times ( 2217 cases vs 18,322 cases) and annual deaths have increased by 9.6 times (4.75 vs 45.83 ) in the recent decade (2011-2022). The mean monthly cases reached a peak in the month of August with 3407.26 cases whereas June-July is the peak transmission season of the dengue virus with the monthly growth factor remaining above one during these two months. In the time series model, we detect an increasing trend of dengue cases in Bangladesh with a much stiffer rise after 2018. Monthly mean temperature (Incidence risk ratio [IRR]: 1.07 (95% CI: 0.90-1.28)), first-lagged rainfall (IRR: 30.31 (95% CI: 29.33-31.33), and second-lagged rainfall (IRR: 12.91 (95% CI: 12.52-13.33) were associated with monthly dengue incidence in Bangladesh.

**Conclusion:** Over two decades, Bangladesh has experimented a significant burden of dengue cases with regular outbreaks and an increasing trend of dengue cases. Global warming, unusual rainfall, urbanization, and population growth might have contributed to this increased incidence of dengue cases in Bangladesh.

**Introduction:**

Dengue is a viral disease that is transmitted to humans by mosquitoes, specifically by the Aedes species [1]. It is caused by four serotypes of the dengue virus (DENV 1-4) and is considered a major global health concern due to its impact on public health [2,3], with an estimated 390 million dengue infections per year, of which 96 million manifests

The first dengue outbreak in Bangladesh was reported in 1964 in East Pakistan, and the term "Dacca fever" was coined. After that, there was a long period of no reported dengue cases 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 [4]. Bangladesh has witnessed a dramatic increase in dengue incidence in recent years, with an estimated 40 million people being infected nationally and 2.4 million annual infections [5]. However, the reported number seems to be only a fraction of these cases[6,7]. Bangladesh witnessed one of the largest dengue epidemics in Bangladesh's history in 2019, with over 101,000 cases and 164 deaths reported (Kayesh et al., 2023). In 2020, the number of cases 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 [7]. In 2021, there was an increase in dengue outbreaks again, with over 28,000 cases and 105 deaths reported [8,9]. In 2022, Bangladesh reported the highest number of dengue-related deaths (n=266) in the country [10]. The 2022 outbreak is characterized by the late onset of the outbreaks with the highest ever reported deaths, partly attributed to the introduction of a new serotype (DENV-4) in the country [7].

The number of dengue cases has been steadily increasing, with significant variations in seasonal patterns and regional distribution. 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) [11]. However, a shift in seasonal patterns has been observed since 2014, with dengue cases being reported during the pre-monsoon season as well [11] . 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 [11]. Climate changes, including changes in rainfall, 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 [11]. This suggests that the dengue transmission season could eventually extend to year-round transmission, with outbreaks occurring at any time.

Identifying trends and seasonality in dengue cases can aid the authorities in Bangladesh in effectively allocating resources to control the spread of the disease. The objective of our study was to i) summarize the annual and monthly cases for the past 22 years by comparing the incidence of cases in the first and decade of this century ii) identify the trend and seasonality of dengue cases and iii) quantify the impact of weather parameters for the monthly incidence of dengue cases in the country.

**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 for the period of January 2000 to December 2022 [10]. We used the case definition of dengue cases used by the Ministry of Health and Family Welfare which was discussed in our earlier article [6]. We collected 3-hourly temperature and daily rainfall data from Bangladesh Meteorological Department (BMD) over the period 2000–2022 [12].

**Statistical analysis**

We performed the analysis of the dengue incidence and meteorological data in several stages. In the first stage, the descriptive statistics were applied to determine the characteristics of confirmed dengue cases and deaths and expressed as mean, minimum, maximum, and standard deviation in each year and also in each month for the entire period. Next, we 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 calculate the monthly growth factor (GF) of dengue cases by 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 [13]. That is,

, where *“Cases”* indicates the number of dengue cases and subscript “t” indicates the current month. To compensate for the occurrence of zeroes in some months, in this equation, we added 1 to the total number of cases for all the months. The GF's distribution was skewed; thus, it was first log-transformed before being further examined.

In the fourth stage, we performed the forecasting model auto-regressive integrated moving average (ARIMA). The ARIMA model is a data-driven, exploratory strategy that enables the user to fit a suitable model based on the data's structure. By removing high-frequency noise from the data, this approach aims to discover local patterns by presuming that the time series values are linearly related. We also conducted a Mann-Kendall (M-K) trend analysis to determine whether any trends existed 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.

Finally, we used a count generalized linear model (GLM) to determine whether the climatic factors are associated to the country's dengue cases over time. The non-normality, heteroscedasticity, and non-linearity that characterize count data were previously considered using GLM. Models for counting time series are appropriately described as dependent between observations and should take into consideration that the observations are nonnegative integers. Using the GLM methodology to model the observations based on historical data is a practical and adaptable strategy [14]. This methodology is implemented by selecting an appropriate link function and distribution for count data. We concentrate on count time series GLM models employing the Poisson link function in this research because they offer a parsimonious way to represent count data [15,16].

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 find any correlation with the predictor’s variable across time, we additionally employed two lagged variables of meteorological elements. After eliminating predictors with high multicollinear relationships, we arrived at average temperature, rainfall (lag 1), and rainfall (lag 2) as the final predictor variables. All these various methods assisted us in reaching a tenable conclusion regarding the trend of dengue incidence and the possible meteorological factors influencing dengue cases in Bangladesh. We used statistical program R, version 3.5.2.2 for the analyses.

**Results:**

Between 2000 and 2022, the mean annual number of dengue cases detected in Bangladesh was 10,619 cases (standard deviation [SD]=23,971). The highest number of annual cases was reported in the year 2019 with 101,354 cases and the highest number of deaths was recorded in 2022 with 281 deaths (Fig 1).

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In the first decade of this century (2000 to 2010), the mean annual number of dengue cases and deaths was 184.72 (SD=436.04) and 0.40 (SD=1.23), respectively **(Fig 1)**. The mean number of dengue annual cases has increased 8 times [1526.83 cases (SD=5462.80)] in the recent decade (2011-2022) and the number of deaths has increased by 9.5 times (3.82 cases [SD=14.83]). The highest number of cases was recorded in the month of August (n=3407) and the lowest in the month of February (7.3 cases) for the period of 2000-2022 **(Fig 1)**.

The average annual temperature was 26.55 °C (SD=3.72) and 26.84 °C (SD=3.76), respectively during the first decade (2000-2010) and the recent decade (2011-2022), respectively. The annual rainfall has decreased by 33.04 mm between two decades (180.08 mm [SD=198.63] vs 147.04 mm [SD=151.32]), respectively (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) | 4.75 (5.68) | 45.83 (91.29) | 0.264 |
| Mean temperature °C (SD) | 26.55 (3.72) | 26.84 (3.76) | <0.001 |
| Mean annual rainfall (SD) | 2160.90 (509.64) | 1764.50 (448.32) | 0.360 |
|  |  |  |  |
|  |  |  |  |

The overall mean GF from month to month was 1.37 (SD=0.86). However, in 4 months (April and July), the monthly GF was above one (95% confidence interval >1), while in the rest of the months, the monthly GF was less than 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 will 3 times higher in the Month of August compared to 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 will be half compared to 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.** 

In the ARIMA model, we detected an increasing trend for the first few years then started to decline. However, we detect a stiff rising of cases after 2018 with an exception of 2020 (the first year of Covid-19 pandemic). In 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 (Figure 2 and Table 2).



**Fig. 2.** Observed and predicted dengue cases using an auto-regressive integrated moving average (ARIMA) model.

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

|  |  |  |
| --- | --- | --- |
| ***Mann-Kendell trend analysis*** | **Non seasonal** | |
|  | **Tau** | **P** |
|  | 0.26 | 0.139 |
| *Sen’s slop test* |  |  |
|  | Sen’s Slope | 95% CI |
|  | 171.67 | -46 to 687 |

In the GLM, the estimated effect of each variable is presented as the incidence risk ratio (IRR). This model suggests that for every degree increase in average temperature per month, the number of cases increased by 7% [IRR=1.07 (95% CI: 0.90-1.28)]. For each additional mm of rainfall in the first lagged month, the number of dengue cases increased by 30 times (IRR=30.31 [95% CI: 29.33-31.33]), and in the second lagged month increased the cases by 12 times [IRR=12.91 (95% CI: 12.52-13.33)]. **(Table 3)**.

Table 3: Relative risks of average temperature and rainfall to Dengue cases in Bangladesh using time-series count Generalized Linear Model.

|  |  |  |
| --- | --- | --- |
|  | IRR (95% CI) | P-value |
| Average temperature | 1.07 (0.90 – 1.28) | 0.441 |
| Rainfall (lag 1) | 30.31 (29.33 – 31.33) | <0.001 |
| Rainfall (lag 2) | 12.91 (12.52 – 13.33) | <0.001 |

**Discussions:**

Dengue fever became an important public health challenge for Bangladesh. The number of cases has increased eight times and deaths by almost 10 times between the first and second decade of this century. During that time the annual temperature increased by 0.33 °C and annual rainfall decreased by 33 mm. Rainfall increases the number of dengue cases significantly in Bangladesh. For each additional mm of rainfall in the previous months (first lagged month), the monthly dengue cases would increase by 30 times in the next month. The monthly growth factor remains above one for only two months (June and July) indicating the number of cases would be more than the current months for these two months.

Two major dengue outbreaks occurred in Bangladesh in the year 2019 and 2022 both characterized by unusual weather patterns and the introduction of two separate serotypes. The 2019 outbreak was characterized by early rainfall and the introduction of a new serotype of DENV-3 in the country [6]. 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 [7].

Seasonality:

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.

**Trend:**

We found an increasing trend of the increasing number of dengue cases and deaths. This trend is associated with climate change in the region associated with increased temperature and natural rainfall. Although the total rainfall decreased in the country the pattern of rainfall changed allowing for longer mosquito breeding.

**Weather pattern:**

We identified the monthly mean temperature along with rainfall of the previous two months had a significant effect on the monthly incidence of dengue cases in Bangladesh. These findings are biologically plausible as rainfall allows the generation of mosquitoes over 30-day windows.

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