**Title: Two Decades of Dengue Outbreaks in Bangladesh (2000-2022): increasing trend of annual cases**

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**Abstract: (Target: 300 words, current count: 264 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 total cases are increasing or not.

**Methods:** We collected monthly reported dengue cases and deaths data from the Ministry’s Health website for the period of 2000-2022 and perform summary statistics. We also perform Sen’s slop test to detect the peak dengue season in Bangladesh.

**Results:** Between 2000 and 2022, Bangladesh's overall annual mean (SD) dengue cases were 884.95 (±4007.44). Compared to the first decade (2000-2010) the annual temperature has increased by 0.29°C and rainfall decreased by 33.04 mm, respectively in the recent decade (2011-2022). During that time dengue cases have increased 8.27 times (184.72 cases vs 1526.80 cases) and dengue-related deaths have increased by 9.55 times (0.40 vs 3.82). The mean monthly cases reach a peak in the month of August with 3407.26 cases. In the time series model, we detect an increasing trend of dengue cases in Bangladesh with a much stiffer rise after 2018. We detected Jul-Sep (1182.48-2034.26) as Bangladesh’s peak season of dengue cases whereas the monthly growth factor remains above one between June and August. Monthly mean temperature (Odds ratio [OR]: 1.07 (95% CI: 0.90-1.28)), first-lagged rainfall (OR: 30.31 (95% CI: 29.33-31.33) and second-lagged rainfall (OR: 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:**

South-East Asia. Dengue is a viral disease that is transmitted to humans by mosquitoes, specifically by the Aedes species (CDC, 2019). 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 (Murray et al., 2013; WHO, 2023a), with an estimated 390 million dengue infections per year, of which 96 million manifest clinically, with any severity of disease (WHO, 2017). In recent decades, the incidence of dengue has increased significantly worldwide (Yang et al., 2021). The World Health Organization (WHO) reported an increase in cases from 505,430 in 2000 to 5.2 million in 2019 (Kraemer et al., 2015; WHO, 2023a). Additionally, a study on the prevalence of dengue estimates that 3.9 billion people in 128 countries are at risk of infection with dengue viruses (WHO, 2017; Shepard et al., 2013; Kayesh et al., 2023).

Dengue has become endemic in more than 100 countries across different regions, including Africa, the Americas, the Eastern Mediterranean, South-East Asia, and the Western Pacific. The most affected regions are the Americas, South-East Asia, and the Western Pacific, with Asia accounting for approximately 70% of the global disease burden (WHO, 2023a). Between 2015 and 2019, the number of dengue cases in the Southeast Asian (SEA) region increased by 46%, from 451,442 to 658,301, while deaths decreased slightly by 2%, from 1,584 to 1,555. Several factors contribute to the spread of dengue mosquitoes and viruses in the SEA region, including rapid population growth, inadequate water supply and storage practices, poor sewer and waste management systems and global warming (WHO, 2023b).

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 (Salje et al., 2019). 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 (Sharmin et al., 2015). The year 2019 witnessed one of the largest dengue epidemics in Bangladesh's history, 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(Haider at al., 2023, JME). . In 2021, there was an increase in dengue outbreaks again, with over 28,000 cases and 105 deaths reported (Hasan et al., 2022; Kayesh et al., 2023). In 2022, an increasing trend of dengue outbreaks was observed in many countries, including Bangladesh, with over 60,000 cases and 266 deaths reported (DGHS, 2022). The 2022 outbreak is characterized by late onset of the outbreaks with the highest ever reported deaths, partly attributed to the introduction of new serotype (DENV-4) in the country (Haider at al 2023., JME).

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) (Mutsuddy et al., 2019). However, a shift in seasonal patterns has been observed since 2014, with dengue cases being reported during the pre-monsoon season as well (Mutsuddy et al., 2019). In particular, 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 (Mutsuddy et al., 2019). 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 (Mutsuddy et al., 2019). 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 seasonality of dengue cases and iii) identify whether dengue cases and deaths are increasing 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 (https://old.dghs.gov.bd/index.php/bd/home/5200) over the period from January 2000 to October 2022. Hospitalized patients with dengue and chikungunya fever are included in DGHS's national surveillance records, which are updated weekly or occasionally daily. Clinical diagnosis with suspected dengue cases' signs and symptoms, such as fever and rash, as well as laboratory tests for the dengue virus (immunoglobulin (IgM or IgG), the dengue virus' non-structural protein 1 (NS1), or just a complete blood count, haematocrit, and platelet counts) are used to determine whether to admit a patient as a dengue patient (<https://www.iedcr.gov.bd/site/page/54072db2-9b03-4481-b88a-adaa47e6d8d7/->, <https://old.dghs.gov.bd/index.php/bd/home/5200>). In order to investigate the relation between weather variables and dengue incidence, monthly temperature and rainfall data were also gathered from Dhaka weather stations by the Bangladesh Meteorological Department (BMD) over the period 2000–2022 (<https://live3.bmd.gov.bd/>).

**Statistical analysis**

The present analysis was conducted in several stages. In the first stage, the descriptive statistics were applied to determine the characteristics of confirmed dengue cases and deaths by using minimum, maximum, mean, and standard deviation in each year and also in each month. In second stage, a comparison was done of dengue cases, deaths, and weather parameters in two decades by using paired sample t-test.

In 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. 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 fourth stage, to determine the trend of dengue cases, we employed 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. A nonparametric test known as the M-K approach can determine whether a trend is monotonous and whether it is positive or negative. The Sen's slope test was also utilized to assess variations in dengue cases (<https://www.sciencedirect.com/science/article/pii/S2772707623000115>, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8176487/>).

Finally, in order to determine whether the climatic factors are associated to the country's dengue cases over time, we used a count generalized linear model (GLM). The non-normality, heteroscedasticity, and non-linearity that characterize count data were previously taken into account using GLM. Models for count time series should appropriately describe the dependency 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 (https://www.jstor.org/stable/2344614?origin=crossref). 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 (<https://www.wiley.com/en-sg/Regression+Models+for+Time+Series+Analysis-p-9780471363552>, https://www.tandfonline.com/doi/abs/10.1198/jasa.2009.tm08270).

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 of 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. The statistical program R, version 3.5.2.2, was used for all analyses.

**Results:**

The mean number of dengue cases detected to have been 884.95 (SD=4007.44) in Bangladesh between January 2000 and December 2022. The lowest mean dengue cases were recorded in 2014, when there were 31.25 (SD=33.27) cases on average, with a range of 0 to 375. Additionally, the mean number of dengue cases was highest in 2019, on that year the mean was 8846.17 (SD=15226.54), with the lowest number being 17 and the highest number being 52636. The mean number of dengue cases in the most recent year (2022) was 5198.50 (SD=7801.19), with a range of 20 to 21932 (Table 1).

Table 1. Summary of annual dengue cases reported in Bangladesh, 2000-2022

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Cases | | |  |
|  | Minimum | Mean (SD) | Maximum | Total |
| 2000 | 0 | 462.58 (684.63) | 2290 | 5551 |
| 2001 | 0 | 202.5 (255.76) | 655 | 2430 |
| 2002 | 0 | 519.33 (1004.11) | 3281 | 6232 |
| 2003 | 0 | 40.5 (108.19) | 372 | 486 |
| 2004 | 0 | 327.83 (460.57) | 1261 | 3934 |
| 2005 | 0 | 87.33 (132.56) | 337 | 1048 |
| 2006 | 0 | 183.33 (314.48) | 972 | 2200 |
| 2007 | 0 | 38.83 (66.92) | 179 | 466 |
| 2008 | 0 | 96.08 (161.2) | 475 | 1153 |
| 2009 | 0 | 39.5 (71.66) | 188 | 474 |
| 2010 | 0 | 34.08 (66.38) | 183 | 409 |
| 2011 | 0 | 113.25 (200.89) | 691 | 1359 |
| 2012 | 0 | 55.92 (81.71) | 262 | 671 |
| 2013 | 0 | 145.75 (177.14) | 495 | 1749 |
| 2014 | 0 | 31.25 (33.27) | 82 | 375 |
| 2015 | 0 | 263.5 (375.09) | 965 | 3162 |
| 2016 | 3 | 505 (588.63) | 1544 | 6060 |
| 2017 | 36 | 230.75 (165.27) | 512 | 2769 |
| 2018 | 7 | 845.67 (1064.1) | 3087 | 10148 |
| 2019 | 17 | 8446.17 (15226.54) | 52636 | 101354 |
| 2020 | 10 | 117.08 (155.13) | 546 | 1405 |
| 2021 | 3 | 2369.08 (3054.99) | 7841 | 28429 |
| 2022 | 20 | 5198.5 (7801.19) | 21932 | 62522 |
| Overall | 0 | 884.95 (4007.44) | 52636 | 244246 |

In the first decade of the twenty-first century, from 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. The average annual temperature and rainfall for the first ten years were 26.55 (SD=3.72) and 180.08 (SD=198.63), respectively. The mean yearly number of cases and fatalities detected over the most recent period [2011-2022] was 1526.83 (SD=5462.80) and 3.82 (SD=14.83), respectively. Recently, the average annual rainfall and temperature were 147.04 (SD=151.32) and 26.84 (SD=3.76), respectively. The mean number of dengue cases, fatalities, and temperatures during the earliest and most recent decades change considerably (P<0.001). However, P>0.001 indicates that there is no significant difference between the first and most recent decade's mean annual rainfall (Table 2).

Table 2: Comparison of dengue cases, deaths, and weather parameters in two decades in Bangladesh.

|  |  |  |  |
| --- | --- | --- | --- |
|  | First decade (2000-2010) | Recent decade (2011-2022) | p-value |
| Mean annual dengue cases | 2216.64 (2123.62) | 18321.92 (31778.90) | 0.219 |
| Mean annual dengue deaths | 4.75 (5.68) | 45.83 (91.29) | 0.264 |
| Mean temperature °C | 26.55 (3.72) | 26.84 (3.76) | <0.001 |
| Mean annual rainfall | 2160.90 (509.64) | 1764.50 (448.32) | 0.360 |
| Mean dengue cases | 184.72 (436.04) | 1526.83 (5462.80) | 0.025 |
| Mean dengue deaths | 0.40 (1.23) | 3.82 (14.83) | 0.030 |

In month wise compilation from 2000 to 2022, the highest number of cases were detected in the month of August with a mean value of 3407.22 cases (SD=10871.65), where lowest in February with a mean value of 7.26 cases (SD=15.21) (Table 3).

Table 3: Mean number of dengue cases in each month (Jan- Dec) for the period 2000-2022

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Dengue Cases** | | |
| Months | Minimum | Mean (SD) | **Maximum** |
| Jan | 0 | 23.57 (49.87) | 199 |
| Feb | 0 | 7.26 (15.21) | 58 |
| Mar | 0 | 6.70 (10.68) | 36 |
| Apr | 0 | 11.17 (20.57) | 73 |
| May | 0 | 30.22 (56.62) | 193 |
| Jun | 0 | 187.65 (406.95) | 1884 |
| Jul | 3 | 1182.48 (3337.07) | 16253 |
| Aug | 4 | 3407.22 (10871.66) | 52636 |
| Sep | 3 | 2034.26 (4083.52) | 16856 |
| Oct | 0 | 1922.78 (4776.24) | 21932 |
| Nov | 0 | 1416.91 (4044.43) | 19334 |
| Dec | 0 | 389.17 (1066.58) | 5024 |

During the study period, the overall mean GF from month to month was 0.02 (SD=1.15). However, only in 2 months (June and July) was the monthly GF significantly >1 while in 6 months (January-February and September-December) this value was negative. More than 70% (32/46) of months between June and July for the period 2000–2022 had mean monthly GF > 1 compared to 10% (23/230) months between August and May of the same period. July showed the highest GF with a mean value of 2.09 (95% CI: 0.97 to 3.20) while January had the lowest value with a mean of -1.88 (95% CI: -2.99 to -0.78) (Fig. 2).

Fig 1: Top: Mean monthly growth factor for the period of 2000-2022. Bottom: The Monthly growth factor for the individual year 2000-2022. 

According to ARIMA model, M-K trend analysis and Sen’s slope test had fair agreement to forecast upcoming dengue cases. ARIMA model showed an increasing trend first few months then started to decline. In M-K trend analysis, we found a positive trend of reported dengue cases (p <0.001 and tau = 0.26) on the basis of previous data. In Sen’s slop test, the slope was 171.67 (95% CI: -46 to 687), which also indicate a upward trend in upcoming months (figure 2 and Table 4).



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

Table 4: 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 |

*RMSE: Root Mean Square Error; MAE: Mean Absolute Error*

In the time-series 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, the relative risk of dengue cases increased by 7% [IRR=1.07 (95% CI: 0.90-1.28)] and for every mm of rainfall in first lagged, the relative risk of dengue cases in Bangladesh increased by 30.31 times [IRR=30.31 (95% CI: 29.33-31.33)] and in second lagged, the relative risk of dengue cases increased by 12.91 times [IRR=12.91 (95% CI: 12.52-13.33)]. Lagged variable of temperature and rainfall without any lag removed from this model because of high multicollinearity (Table 5).

Table 5: Relative risks of average temperature and rainfall to Dengue cases in Bangladesh using time-series GLM methods

|  |  |  |
| --- | --- | --- |
|  | 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 annual temperature increased by 0.33 C and annual rainfall decreased by 33 ml. Two major outbreaks occurred in 2019 and 2022 both characterized by unusual weather patterns and the introduction of new serotypes. The 2019 outbreak was characterized by early rainfall and the introduction of a new serotype of DENV-3 in the country (Ahsan et al 2020). The 2022 outbreak was characterized by the late onset of rainfall and prolongation of monsoon along with the introduction of new serotype, DENV-4 in the country.

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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