OXFORD UNIVERSITY PRESS | Journal of Medical Entomology

Two Decades of Endemic Dengue in Bangladesh (2000-2022): Trends, Seasonality, and Impact of Temperature and Rainfall Patterns on Transmission Dynamics

Journal:	*Journal of Medical Entomology*
Manuscript ID	JME-2023-0210.R3
Manuscript Type:	Research
Date Submitted by the Author:	n/a
Complete List of Authors:	Hasan, Mohammad Nayeem; Shahjalal University of Science and Technology, Department of Statistics Khalil, Ibrahim; Government of the People's Republic of Bangladesh Ministry of Fisheries and Livestock, Department of Livestock Services Chowdhury, Muhammad Abdul Baker; University of Florida College of Medicine, Department of Neurosurgery Rahman, Mahbubur; University of London, Institute of Epidemiology; Ministry of Health and Family Welfare, Institute of Epidemiology Asaduzzaman, Md; Staffordshire University, Technologies, and Arts Billah, Masum; Staffordshire University, Technologies, and Arts Banu, Laila Arjuman; Bangabandhu Sheikh Mujib Medical University, Department of Anatomy Alam, Mahbub-Ul; International Centre for Diarrhoeal Disease Research Bangladesh, Environmental Intervention Unit Ahsan, Atik; International Centre for Diarrhoeal Disease Research Bangladesh, Environmental Intervention Unit Traore, Tieble; WHO, Emergency Preparedness and Response Programme Uddin, Md. Jamal; Shahjalal University of Science and Technology, Department of Statistics; Daffodil International University, Department of General Educational and Development Galizi, Roberto; Keele University, School of Life Sciences Russo, Ilaria; Keele University, School of Medicine Zumla, Alimuddin; University College London, Division of Infection and Immunity; University College London Hospitals NHS Foundation Trust, Division of Infection and Immunity Haider, Najmul; Keele University, School of Life Sciences
Please choose a section from the list:	Modeling/GIS, Risk Assessment, Economic Impact
Field Keywords:	Public Health Entomology, Mosquito Borne Diseases
Organism Keywords:	Aedes aegypti

Two Decades of Endemic Dengue in Bangladesh (2000-2022): Trends, Seasonality, and Impact of Temperature and Rainfall Patterns on Transmission Dynamics

Mohammad Nayeem Hasan[1], Ibrahim Khalil [2], Muhammad Abdul Baker Chowdhury [3], Mahbubur Rahman [4,5], Md Asaduzzaman [6], Masum Billah [6], Laila Anjuman Banu [7], Mahbub-ul Alam[8], Atik Ahsan [8], Tieble Traore [9], Md. Jamal Uddin[1,10] Roberto Galizi [11], Ilaria Russo[12], Alimuddin Zumla[13], Najmul Haider[11*]

[1] Department of Statistics, Shahjalal University of Science and Technology, Sylhet 3114, Bangladesh (MNH: nayeem5847@gmail.com, MJU: jamal-sta@sust.edu)

[2] Department of Livestock Services, Ministry of Fisheries and Livestock, Bangladesh, Dhaka, Bangladesh (IK: dribrahim.dls@gmail.com)

[3] Department of Neurosurgery, University of Florida College of Medicine, Gainesville, Florida FL 32610, USA (MABC: baker.chowdhury@neurosurgery.ufl.edu)

[4] The Royal Veterinary College, University of London, Hawkshead Lane, North Mymms, Hatfield, Hertfordshire, United Kingdom (Email: MR: dr_mahbub@yahoo.com)

[5] Institute of Epidemiology, Disease Control and Research (IEDCR), Ministry of Health and Family Welfare, Mohakhali, Dhaka, Bangladesh (MR: dr_mahbub@yahoo.com)

[6] School of Digital, Technologies, and Arts, Staffordshire University, Staffordshire, UK (MB: masum.billah@staffs.ac.uk , MA: Md.Asaduzzaman@staffs.ac.uk)

[7] Department of Anatomy, Bangabandhu Sheik Mujib Medical University, Dhaka, Bangladesh (dr.lailabanu@gmail.com)

[8] Environmental Intervention Unit, International Centre for Diarrhoeal Diseases Research, Bangladesh (ICDDR,B), Dhaka-1212, Bangladesh (MUA: mahbubalam@icddrb.org, AA: atik.ahsan@icddrb.org)

[9] Emergency Preparedness and Response Programme, WHO Regional Office for Africa, Dakar Hub, Daker, Senegal (TT: traoret@who.int)

[10] Department of General Educational and Development, Daffodil International University, Dhaka, Bangladesh (MJU: jamal-sta@sust.edu)

[11] School of Life Sciences, Faculty of Natural Sciences, Keele University, Keele, Staffordshire, United Kingdom, ST5 5BG (NH: n.haider@keele.ac.uk, RG: r.galizi@keele.ac.uk).

[12] School of Medicine, Faculty of Medicine and Health Sciences, Keele University, Staffordshire, ST5 5BG, United Kingdom (IR: i.russo@keele.ac.uk)

[13] Division of Infection and Immunity, Centre for Clinical Microbiology, University College London and NIHR-BRC, University College London Hospitals, London, United Kingdom (AZ: a.zumla@ucl.ac.uk).

***Corresponding author (NH):** Dr Najmul Haider, School of Life Sciences, Keele University, Huxley Building, Room 122, Keele, Staffordshire, ST5 5BG, United Kingdom, Email: n.haider@keele.ac.uk , Phone : **(+44) 01782 734414**

Abstract:

Background: The objectives of this study were to compare dengue virus (DENV) cases, deaths, case-fatality ratio, and meteorological parameters between the first and the recent decade of this century (2000-2010 vs. 2011-2022) and to describe the trends, seasonality, and impact of change of temperature and rainfall patterns on transmission dynamics of dengue in Bangladesh

Methods: For the period 2000-2022, dengue cases and death data from Bangladesh's Ministry of Health and Family Welfare's website, and meteorological data from the Bangladesh Meteorological Department were analyzed. A Poisson regression model was performed to identify the impact of meteorological parameters on the monthly dengue cases. A forecast of dengue cases was performed using an autoregressive integrated moving average model.

Results: Over the past 22 years, a total of 244,246 dengue cases were reported including 849 deaths (Case fatality ratio [CFR] =0.34%). The mean annual number of dengue cases increased eight times during the second decade, with 2,216 cases during 2000-2010 vs. 18,321 cases during 2011-2022. The mean annual number of deaths doubled (21 vs. 46), but the overall CFR has decreased by one-third (0.69% vs 0.23%). Concurrently, the annual mean temperature increased by 0.49 °C, and rainfall decreased by 314 mm with altered precipitation seasonality. Monthly mean temperature (Incidence risk ratio [IRR]: 1.26), first-lagged rainfall (IRR: 1.08), and second-lagged rainfall (IRR: 1.17) were significantly associated with monthly dengue cases.

Conclusions: The increased local temperature and changes in rainfall seasonality might have contributed to the increased dengue cases in Bangladesh.

Keywords: Dengue, Bangladesh, Climate change, Temperature, Rainfall

Introduction:

Dengue fever is a mosquito-borne disease (MVD) caused by four distinct serotypes of the dengue virus (DENV) within the family *Flaviviridae* (Simmonds et al. 2017). DENV is transmitted to humans by bites of *Aedes aegypti* (L.) and *Aedes albopictus* (Skuse) (WHO 2009; CDC 2019). DENV is endemic in over 125 countries, and the number of cases globally reported to WHO continues to increase yearly (Bhatt et al. 2013; WHO 2023). Annually, an estimated 390 million dengue infections are estimated worldwide, including 96 million clinical cases making DENV one of the most important vector-borne diseases (VBDs) (Murray et al. 2013; Messina et al. 2019; WHO 2023). Most infections (>80%) are self-limiting with no or mild clinical manifestation resulting in lifelong immunity for that serotype (WHO-Bangladesh 2022). However, reinfection with different serotypes, known as secondary or tertiary dengue infection, may result in severe dengue with an increasing risk of fatal outcome (Teo et al. 2023). Currently, South and Southeast Asia are ‘hotspots’ of DENV infection, with more than 50% of cases recorded in these regions (WHO South-East Asia 2023). The first DENV 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). Over the past few years, the number of dengue cases has been steadily increasing, with significant seasonal and regional variation. Analysis of data from 2000 to 2017 revealed that almost half of the dengue cases occurred during the monsoon (May-August) and the post-monsoon (September-December) seasons (Mutsuddy et al. 2019). Historically the monsoon has been the primary dengue transmission season in Bangladesh, although the number of dengue cases has increased during the post-monsoon season in recent years (Haider et al. 2021; Hossain et al. 2023).

Bangladesh’s hot and humid weather favors the production of a large variety of mosquito species with more than 123 species listed in 2016 (Irish et al. 2016; Bashar et al. 2016). The most common vectors of dengue virus, *Ae aegypti* and *Ae albopictus,* were first recorded in 1952 (Asir-Ud-Din M 1952) and recent studies in Dhaka showed a higher Breteau index which measures the number of positive containers per 100 households: 30.8 in 1997, 24.6 in 2000, 55.8 in 2011, 28.7 in 2012 and 22.5 in 2013 (Ferdousi et al. 2015; Paul et al. 2018). In 2022, the maximum Breteau index of >50 was recorded for six wards of the Dhaka South City Corporation area (Tawsia Tajmim 2022). The pupal index (PI) which measures the number of pupae per 100 houses was estimated during the monsoon season in several years in Bangladesh: 62.2 in 2011, 153.5 in 2012, and 75.9 in 2013. However, during the dry period, the PI was estimated as 16.7 in 2012 (Paul et al. 2018).

Climate change, including changes in precipitation, temperature and humidity, as well as rapid unplanned urbanization, were identified as strong indicators of an ecological imbalance that has led to an increase in dengue cases in Bangladesh (Mutsuddy et al. 2019). These changes could eventually extend dengue transmission season year-round, with a chance of outbreaks occurring at any time of the year. Identifying trends and seasonality in dengue cases may aid health authorities and relevant public and private administrations in effectively allocating resources to control the spread of the DENV through vector control. The objectives of our current study were to: i) compare the annual and monthly number of dengue cases and deaths between 2000 and 2022, ii) identify the overall trend and seasonality of dengue cases, iii) quantify the impact of weather parameters on the number of monthly dengue cases, and iv) forecast the annual number of dengue cases for the next decade.

Methods:

Data sources:

The current dengue surveillance in Bangladesh is coordinated by the Management Information System (MIS) of the Ministry of Health and Family Welfare of Bangladesh (Haider et al. 2023 Sep). The surveillance includes hospitalized patients diagnosed as infected with dengue virus primarily from government hospitals except in the capital city Dhaka, where more than 57 private hospitals are included in addition to 20 public hospitals. Outside the capital city Dhaka, the central district hospital of 64 districts and medical college hospitals are also included in the surveillance system. We collected data on the number of reported dengue cases and deaths from the publicly shared database of the MIS from January 2000 to December 2022. The Ministry of Health and Family Welfare, Bangladesh defines dengue cases based on clinical symptoms (including fever and rash) and/or laboratory tests for IgM or IgG antibodies to DENV and nonstructural 1 protein (NS-1) of DENV (Ahsan et al. 2021).

We used three-hourly temperature and daily rainfall data from the Bangladesh Meteorological Department (BMD) over the period 2000–2022 from the meteorological station located in Mirpur, Dhaka (Lat 23.46, Lon 90.23). Given Bangladesh's relatively small land size and moderate climate variation across the country, we focused data solely on the Dhaka station. Furthermore, a substantial proportion of historical dengue cases (>90%) have originated from Dhaka city (Sharmin et al. 2018).

Procedures

The monthly number of reported dengue cases was used as the primary outcome variable. Two weather variables, temperature, and rainfall were used as the covariates for the regression analysis. In addition, monthly rainfall lagged by 1 or 2 preceding months was also used as predictors for the number of monthly dengue cases.

Statistical analysis

We analyzed the monthly dengue cases and meteorological data for the period of 2000-2022. We used 2010 (the median year) to divide the period 2000-2022. Then, we compared the number of dengue cases, deaths, and weather parameters during the two decades (2000-2010 and 2011-2022) using a paired sample t-test, aimed at comparing trends, developments, and changes between these periods. In the first stage, descriptive analyses were conducted to determine the characteristics of dengue cases and deaths, with mean and interquartile range (IQR) in each year and each month calculated for the entire period. Next, we calculated the monthly growth factor (GF) of dengue cases by dividing the number of dengue cases reported in each month by the number of dengue cases reported in the previous month and repeating this process for each month from 2000 to 2022 (Haider et al. 2021). The formula for the growth factor can be given by

$$GF_t = \frac{N_{t+1} + 1}{N_t + 1}$$

where N_t indicates the number of dengue cases in t^{th} month. To avoid the occurrence of zeros in some months, we added 1 to the total number of cases for each month. The distribution of the GF was skewed; therefore, we used the natural log transformation before the data was further examined. However, we have also performed a reverse transformation of the log (GF) values by back-transforming values to the original scale for ease of interpretation (Haider et al. 2021). A monthly GF greater than 1 indicates that the number of dengue cases would be more than the number of dengue cases of the previous month, while a GF less than 1 means that the number of dengue cases in a new month would be less than the previous month. For example, if there are 100 cases in January, the number of dengue cases in February would be 200 when the value of GF is 2.0 or 50 cases when the value of GF is 0.5 in January (Haider et al. 2021)

We performed forecasting using the autoregressive integrated moving average (ARIMA) model. The ARIMA model is a data-driven, exploratory strategy that enabled us to fit a suitable model and forecast values. The ARIMA model consists of autoregressive (p) terms, differencing (d) terms, and moving average (q) operations, and it is denoted as ARIMA (p, d, q) (Kumar and Susan 2020). To select the appropriate autoregressive and moving average orders, the autocorrelation function (ACF) and partial autocorrelation function (PACF) were examined. Additionally, the differencing parameter, represented by "d," indicated the number of times the time series was different to achieve stationarity (Hasan et al. 2021). 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 possible upward or downward trends (Yue and Pilon 2004). The null hypothesis posits no monotonic trend, while the alternative hypothesis suggests the presence of a trend, which could be positive, negative, or non-null. We also performed Sen's slope test to assess variations in annual dengue cases and deaths. The slope greater than 0 indicates an upward trend and less than 0 indicates a downward trend of a given period (Sen 1968).

We then used a time series count generalized linear model (GLM), more specifically, a time-series Poisson regression model, to determine whether the meteorological factors were associated with the change in dengue cases over time (Sumi et al. 2021). Monthly dengue cases were utilized as the outcome variable in this model predicted by temperature and rainfall data from the Bangladesh Meteorological Department (BMD). We have estimated the degree-hour of heat generated by the addition temperature each year in Bangladesh. To compare this with the extrinsic incubation period (EIP) of the dengue virus in *Aedes* mosquito, we estimated the degree-hour required to complete the extrinsic incubation period (EIP) at 26° C using the mathematical formula [-0.1393 + 0.008*Temp] presented by Focks et al. (1995). We used the statistical program RStudio, version 3.5.2.2 for the analyses (R Core Team 2022).

Results:

Between 2000 and 2022, DGHS reported a total of 244,246 dengue cases, with an annual mean of 10,619 cases (interquartile range [IQR]: 859.5-5,805.5), including 849 fatal outcomes with a case-fatality ratio (CFR) of 0.34%. Between 2000 to 2010, the mean annual number of dengue cases was 2,216 (IQR: 480-3182) which increased by 8 times in the following decade (2011-2022) at 18,321 (IQR: 1405-28429, p=0.22) **(Table 1)**. Between these two periods, the mean number of annual deaths due to DENV cases increased by 2.2 times, from 21.2 to 46.6 cases (p=0.85). However, the CFR of DENV cases decreased slightly from 0.69% to 0.23% (p=0.08) (**Table 1**).

The highest monthly average number of cases was recorded in August (n=3,407 cases) and the lowest was in March (n=6.7 cases) **(Fig 1B)**. The highest number of annual cases was reported in 2019 with 101,354. The highest number of deaths was recorded in 2022 with 281 deaths, which was 35% of total deaths recorded in the past 23 years in Bangladesh **(Fig 1)**. Most (65%, n=550) dengue-related deaths were recorded after 2018 **(Fig 1)**.

The average annual temperature was 26.35 °C (SD=0.49) during the first decade (2000-2010) and 26.84 °C (SD=0.37) during the recent decade (2011-2022) (**Table 1**). The increase of 0.49° C temperature was equivalent to 4,292 degree-hours/year of heat (365 days X 24 hours X 0.49° C). For dengue virus transmission, approximately 349-degree-hours of equivalent heat is needed to complete the EIP of DENV in the *Aedes* mosquito at 26° C (Focks et al. 1995). The annual total rainfall decreased by 314 mm between the two decades, from 2078.6 mm to 1764.5 mm

(**Table 1**), of which 308 mm decreased during the monsoon (July-October) season and only 6 mm decreased during the non-monsoon period. However, during pre-and-post monsoon season, rainfall (more than 3rd quantile value of monthly rainfall for the decade) increased in the second decade **(Fig 2)**.

The overall mean GF for the number of dengue cases per 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 for 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. June had the highest GF with a mean value of 3.47 indicating that cases would be more than 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 nearly halved compared to the number of cases recorded in December (**Fig. 3**).

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) with a tau value of 0.26 and p-value of 0.14 indicating a non-significant upward trend.

In the GLM, the estimated effect of each variable is presented as the incidence risk ratio (IRR). The model indicates that dengue cases would rise by 26% with a one-degree centigrade (°C) temperature increase. 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: 1.08-1.09]), and in the second lagged month increases in cases would be by 17% [IRR=1. 17 (95% CI: 1. 17 -1.18)].

In the ARIMA model, we detected an increasing trend for the first few years, which then started to decline. However, a strong rise in cases was observed after 2018 except for 2020 (the first year of the COVID-19 pandemic). The forecasted value showed a flat line with reduced variation over time in the number of dengue cases in Bangladesh **(Fig 4)**.

Discussion:

Dengue is currently an important public health challenge for Bangladesh. Our analysis showed that the number of DENV cases has increased eight times, deaths have doubled, and the CFR dropped to one-third between the first and second decades of this century. Between these periods, the annual temperature increased by 0.49°C, and annual rainfall decreased by 314 mm, despite changes in the seasonality of rainfall with unusually early or late rainfall outside the typical monsoon season (July-October) (Haider et al. 2014). The monthly growth factor remained above one for four months (April to July) which overlapped the hot and humid period of the year. Monthly mean temperature, monthly first-lagged rainfall, and second-lagged rainfall played a critical role in monthly dengue cases in Bangladesh.

The average increase of 0.49°C temperature added approximately 4,292-degree-hours of equivalent heat per year. This additional heat would favor vector borne disease (VBD) transmission. For DENV, approximately 349-degree-hours equivalent heat is needed to complete the EIP in *Aedes* mosquitoes at 26° C (Focks et al. 1995). Therefore, the addition of 0.49°C temperature shortens the duration of the EIP and thus increases the rate of virus dengue transmission. An 8-fold increase in dengue cases is a possible indication of the impact of increases in temperature in the country. Our model identified a significant role of monthly mean temperature, with an additional 1°C temperature increasing the monthly cases by 26%. Earlier studies showed that for every 1°C increase in temperature, dengue cases increased by 61% in Australia, 12-22% in Cambodia, 5% in Vietnam, and 2.6% in Mexico (Soneja et al. 2021).

Increasing temperatures can accelerate mosquito population growth and shorten the duration of the EIP of the virus, thereby allowing an increased the biting rate and more frequent transmission (Najmul Haider 2018; Couper et al. 2021). Decreased rainfall can increase the risk of dengue, especially in urbanized areas that may have an inadequate and intermittent water supply during drought (Lowe et al. 2021).

Rainfall provides oviposition and larval developmental sites and thereby plays an important role in mosquito population size and pathogen transmission. Although we found a 15% reduction in annual rainfall in the recent decade from the immediate past decade, we detected an increase in rainfall during pre-and-post monsoon seasons, thereby extending the season for mosquitoes and other arthropod vectors. Our model showed that the first and second lagged month's rainfall increased monthly cases by 8% and 17%, respectively. These findings were consistent with earlier studies in Bangladesh that showed that peak dengue cases occurred two months after peak rainfall (Salje et al. 2016) or an additional rainy day per month increased dengue cases by 6% in the succeeding month (Rahman et al. 2020). Similar findings were reported in Vietnam with dengue cases being associated with both first and second-lagged months (Cuong et al. 2011). In the greater part of the capital city Dhaka, there is a shortage of municipal water, and thus people attempt to store municipal water when available as well as rainwater. This might facilitate the production of *Aedes* mosquitoes (Akanda et al. 2020). In Timor-Leste, a 47% increase in dengue cases was recorded with an additional 1 mm seasonal rainfall increase (Wangdi et al. 2018). These findings are biologically plausible as altered precipitation during pre- and post-monsoon allows extended vector seasons facilitating additional human cases (Yuan et al. 2020).

Bangladesh's dengue season is characterized by hot and wet periods from June to August. This is the period with the highest amount of rainfall facilitating *Aedes* abundance (Haider et al. 2023

May 18). The monthly mean growth factor above 1 for April – June indicates that for each of these months, the number of dengue cases will surpass the previous month. Thus, we suggest starting vector control intervention in April in Bangladesh.

Two large dengue outbreaks occurred in Bangladesh in 2019 and 2022, with both characterized by unusual weather patterns and the occurrence of two different DENV serotypes. The 2019 outbreak was characterized by early rainfall of 120 mm in February compared to a historical monthly mean of 20 mm precipitation, along with the introduction DENV-3 (Ahsan et al. 2021). The 2022 outbreak was characterized by the late onset of rainfall, with 297 mm of rainfall in October compared to a monthly mean of 156 mm that may have prolonged the vector transmission season and by the introduction of DENV-4 (Haider et al. 2023 May 18). The introduction this new serotype exposed a largely naïve population in a densely populated country like Bangladesh. A large proportion of the population had already been infected with one or more serotypes of DENV with more than 80% of people living in Dhaka having antibodies against DENV (Salje et al. 2016). Another study predicted an estimated 40 million people had been infected with DENV nationally, with 2.4 million annual infections (Salje et al. 2019). Thus, any subsequent infections raise the risk of developing severe dengue hemorrhagic fever through antibody-dependent enhancement (ADE) (Teo et al. 2023). The deaths of many people in 2022 when DENV-4 was introduced were probably associated with secondary and/or tertiary DENV infection (Haider et al. 2023 May 18).

Our analysis shows that there was a significant monotonic increasing trend of dengue cases in Bangladesh for the period 2000-2022 (M-K trend test); however, the magnitude of the increasing trend was not significant (Sen's Slope test). This might be due to the large variation of the cases reported in different years. For example, more than 82% of dengue cases (n=202,425) that were recorded in the last 23 years (2000-2023) were reported in the recent five years (2018-2022). The increase in case reporting in recent years might be a true increase in dengue cases or could be the result of the development of the health care system, improved diagnostic system, and inclusion of more hospitals in the surveillance system in Bangladesh (Haider et al. 2023 Sep).

Controlling vector-borne diseases in tropical countries where temperatures, humidity, and rainfall remain favorable for mosquitoes during most of the year is a difficult task (Haider et al. 2023 May 18). Concerns have been raised over the development of insecticide resistance (Al-Amin et al. 2020; Ahsan et al. 2021) and the failure of developing a successful dengue vaccine (Wang et al. 2017). The prospect of *Wolbachia*-related intervention is still far from being applied on a national scale considering the expenses and associated technicalities. In this situation, an integrated and holistic vector management plan engaging the local communities is key for controlling *Aedes*-borne diseases, especially in resource-limited countries. Regular destruction of mosquito developmental sites and increasing surveillance for detecting active cases are key to limiting dengue virus infections. The development of a municipal water system that would preclude the need to store water is essential to prevent *Aedes* mosquito production. Continuous active surveillance for DENV cases will enable early detection of cases and the location of outbreaks. Public health authorities will be able to identify areas where the disease is spreading, take immediate action to control mosquito populations, isolate infected patients, and implement public awareness campaigns to educate people about preventive measures. Early detection and response can help prevent the further spread of the disease and reduce its impact.

Several weaknesses may have impacted our study. We relied on the reported number of cases from the Ministry of Health and Family Welfare's website, which mainly relies on passive reporting systems from the selected health facilities in the country (Ahsan et al. 2021). These numbers seem to underestimate the actual number of infections and fever cases. The hospitals included in the surveillance system are only a small fraction of total healthcare facilities in Bangladesh (~5%) where dengue patients can seek healthcare (Haider et al. 2023 Sep). A modeling study based on the national seroprevalence of DENV antibodies predicted an annual infection of 2.4 million people (Salje et al. 2019). Dengue cases similarly are underestimated globally as it is difficult to detect asymptomatic or mild cases that never reach healthcare settings. Although mild cases are missed frequently, severe and fatal cases would likely visit the hospital and thus be counted as numerators in our estimates. Thus, our estimation did not overlook the worst-case scenario, but may have estimated a higher CFR because of the underestimation of the denominators. Another limitation pertains to our exclusive utilization of weather data from the Dhaka station. Given Bangladesh's relatively small size and the moderate climate variation across the country, we focused our data collection solely on the Dhaka station. Furthermore, a substantial proportion of historical dengue data originates from Dhaka city. We could not use herd immunity data in our model as these data are not available for different serotypes of DENV in Bangladesh. However, earlier studies show that people living in the capital city and larger cities like Chittagong have higher seroprevalence compared to rural areas where the seroprevalence was as low as 3% (Salje et al. 2019). This also illustrates a high risk of antibody-dependent enhancement (ADE) through secondary and tertiary infection in large cities. We accept that the increase in dengue cases in the recent decade could be a result of multiple factors that we could not include in the analysis. These factors include the improvement of the healthcare system which now detects a greater proportion of clinical cases than in the past, the arrival of new serotypes of DENV, and the increased size of the urban population.

Conclusions:

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 may partly be explained by global warming, with an increase of 0.49°C annual temperature as well as changes in duration and length of the rainy season. Unusual early or late rain in and beyond the monsoon season likely contributed to extending the length of the dengue transmission season in Bangladesh. The monthly mean temperature and monthly total rainfall of the first-lagged month and second-lagged months showed a large influence on the monthly DENV cases in Bangladesh. The mean monthly growth factor remained significantly above one during April-July, which coincided with the hot and rainy season of the country indicating an earlier vector control would benefit the country.. We recommend an integrated and holistic vector management plan engaging local communities in the elimination of mosquito larval habitats and increasing surveillance for detecting active dengue cases. Proactive surveillance, vector control, and community engagement remain essential public health interventions. In the context of climate change, urbanization, trade, and the movement of infected people, there is a need to operationalize the One Health approach to address dengue fever and other vector-borne diseases in Bangladesh and beyond.

Acknowledgments:

We are grateful to the Ministry of Health and Family Welfare of Bangladesh for publicly sharing the dengue cases and deaths data. We acknowledge the Bangladesh Meteorological Department for sharing the meteorological data. NH, and AZ, are part of the PANDORA-ID-NET Consortium (EDCTP 373 Reg/Grant RIA2016E-1609) funded by the European and Developing Countries Clinical Trials Partnership (EDCTP2) program. NH is a member of the International Development Research Centre, Canada's grant on West African One Health Actions for understanding, preventing, and mitigating outbreaks (109810-001). AZ is a National Institutes of Health Research senior investigator, and a Mahathir Science Award and Pascoal Mocumbi Award laureate.

Author contribution statement: NH ideated the study and all authors helped develop the study outline and protocol. MNH and IK collected the data. NH, MNH, MA and AZ analyzed the data. NH, IK and MNH prepared the first draft manuscript and all authors contributed to several drafts and finalization of the manuscript. All authors approved the final draft and submission of the manuscript.

Financial Support: There was no funding for this research.

Conflict of interest: The authors declare that they have no conflict of interest.

Ethics statement: This study does not include individual-level data and thus does not require ethical approval. We used publicly available data on Dengue cases and deaths.

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/).

References

Ahsan A, Haider N, Kock R, Benfield C. Possible Drivers of the 2019 Dengue Outbreak in Bangladesh: The need for a robust community-level surveillance system. J Med Entomol, 2021: 58(1):37–39. doi:10.1093/jme/tjaa150.

Akanda AS, Johnson K, Ginsberg HS, Couret J. Prioritizing water security in the management of vector-borne diseases: Lessons from Oaxaca, Mexico. Geohealth, 2020: 4(3). doi:10.1029/2019GH000201.

Al-Amin HM, Johora FT, Irish SR, Hossainey MRH, Vizcaino L, Paul KK, Khan WA, Haque R, Alam MS, Lenhart A. Insecticide resistance status of *Aedes aegypti* in Bangladesh. Parasit Vectors,2020: 13(1):622. doi:10.1186/s13071-020-04503-6.

Asir-Ud-Din M. Mosquitoes breeding in tree-holes and bamboo stumps in Dacca (East Pakistan). 1952: 2: 110–112. Pakistan Journal of Health. 2:110–112.

Bashar K, Rahman MdS, Nodi IJ, Howlader AJ. Species composition and habitat characterization of mosquito (Diptera: Culicidae) larvae in semi-urban areas of Dhaka, Bangladesh. Pathog Glob Health. 2016: 110(2):48–61. doi:10.1080/20477724.2016.1179862.

Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, Drake JM, Brownstein JS, Hoen AG, Sankoh O, Myers MF, George DB, Jaenisch T, Wint GRW, Simmons CP, Scott TW, Farrar JJ, Hay SI. The global distribution and burden of dengue. Nature. 2013: 496(7446):504–7. doi:10.1038/nature12060.

CDC. 2019. Transmission through mosquito bites. [accessed 2023 May 15]. https://www.cdc.gov/dengue/transmission/index.html.

Couper LI, Farner JE, Caldwell JM, Childs ML, Harris MJ, Kirk DG, Nova N, Shocket M, Skinner EB, Uricchio LH, Exposite-Alonso M, Mordecai EA. How will mosquitoes adapt to climate warming? Elife. 2021:10. doi:10.7554/eLife.69630.

Cuong HQ, Hien NT, Duong TN, Phong TV, Cam NN, Farrar J, Nam VS, Thai KTD, Horby P. 2011. Quantifying the Emergence of Dengue in Hanoi, Vietnam: 1998–2009. PLoS Negl Trop Dis. 5(9):e1322. doi:10.1371/journal.pntd.0001322.

Ferdousi F, Yoshimatsu S, Ma E, Sohel N, Wagatsuma Y. Identification of Essential Containers for Aedes Larval Breeding to Control Dengue in Dhaka, Bangladesh. Trop Med Health. 2015: 43(4):253–64. doi:10.2149/tmh.2015-16.

Focks DA, Daniels E, Haile DG, Keesling JE. A simulation model of the epidemiology of urban dengue fever: Literature analysis, model development, preliminary validation, and samples of simulation results. Am J of Trop Med and Hyg. 1995: doi:10.4269/ajtmh.1995.53.489.

Haider N, Asaduzzaman M, Hassan MN, Rahman M, Sharif AR, Ashrafi SAA, Lee SS, Zumla A. 2023 Sep. Bangladesh's 2023 Dengue outbreak – age/gender-related disparity in morbidity and mortality and geographic variability of epidemic burdens. Int. J. Inf. Dis.. 2023. doi:10.1016/j.ijid.2023.08.026.

Haider N, Chang Y-M, Rahman M, Zumla A, Kock RA. 2021. 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. Current Res. in Parasitol. Vector-Borne Dis. 1:100063. doi:10.1016/j.crpvbd.2021.100063.

Haider N, Hasan MN, Khalil I, Tonge D, Hegde S, Chowdhury MAB, Rahman M, Hossain Khan M, Ansumana R, Zumla A, Uddin MJ . The 2022 dengue outbreak in Bangladesh: hypotheses for the late resurgence of cases and fatalities. J Med Entomol. 2023. doi:10.1093/jme/tjad057.

Haider N, Rahman MS, Khan SU, Mikolon A, Gurley ES, Osmani MG, Shanta IS, Paul SK, Macfarlane-Berry L, Islam A, Desmon J, Epstein JH, Daszak P. Azim T. Luby SP, Zeidner NZ, Rahman MZ. . Identification and Epidemiology of a Rare HoBi-Like Pestivirus Strain in Bangladesh. Transbound Emerg Dis. 2014. 61(3):193–198. doi:10.1111/tbed.12218..

Hasan MN, Haider N, Stigler FL, Khan RA, McCoy D, Zumla A, Kock RA, Uddin MJ. The Global Case-Fatality Rate of COVID-19 Has Been Declining Since May 2020. Am J Trop Med Hyg. 2021.104(6):2176–2184. doi:10.4269/ajtmh.20-1496.

Hossain MS, Noman A Al, Mamun SA Al, Mosabbir A Al. Twenty-two years of dengue outbreaks in Bangladesh: epidemiology, clinical spectrum, serotypes, and future disease risks. Trop Med Health. 2023. 51(1):37. doi:10.1186/s41182-023-00528-6.

Irish SR, Al-Amin HM, Alam MS, Harbach RE. A review of the mosquito species (Diptera: Culicidae) of Bangladesh. Parasit Vectors. 2016. 9(1):559. doi:10.1186/s13071-016-1848-z.

Kumar N, Susan S. 2020. COVID-19 Pandemic Prediction using Time Series Forecasting Models. In: 11th International Conference on Computing, Communication and Networking Technologies (ICCCNT). IEEE. 2020. p. 1–7.

Lowe R, Lee SA, O'Reilly KM, Brady OJ, Bastos L, Carrasco-Escobar G, de Castro Catão R, Colón-González FJ, Barcellos C, Carvalho MS, Blangiardo M, Rue H, Gasparrini A. . Combined effects of hydrometeorological hazards and urbanisation on dengue risk in Brazil: a spatiotemporal modelling study. Lancet Planet Health. 2021. 5(4):e209–e219. doi:10.1016/S2542-5196(20)30292-8.

Messina JP, Brady OJ, Golding N, Kraemer MUG, Wint GRW, Ray SE, Pigott DM, Shearer FM, Johnson K, Earl L, Marczak LB, Shirude S, Weaver ND, Gilbert M, Velayudhan R, Jones P, Jaenisch T, Scott TW, Reiner RC, Hay SI . The current and future global distribution and population at risk of dengue. Nat Microbiol. 2019. 4(9):1508–1515. doi:10.1038/s41564-019-0476-8.

Murray NEA, Quam MB, Wilder-Smith A. Epidemiology of dengue: past, present and future prospects. Clin Epidemiol. 2013. 5(1):299–309. doi:10.2147/CLEP.S34440.

Mutsuddy P, Tahmina Jhora S, Shamsuzzaman AKM, Kaisar SMG, Khan MNA, Dhiman S. Dengue Situation in Bangladesh: An Epidemiological Shift in terms of Morbidity and Mortality. Can J Infect Dis Med Microbiol. 2019. doi:10.1155/2019/3516284.

Najmul Haider. Modeling the vector-borne disease transmission potential in northern Europe with a special emphasis on microclimatic temperature: PhD Thesis. 2018. [Lyngby]: Technical University of Denmark. [accessed 2023 Nov 28]. https://orbit.dtu.dk/en/publications/modeling-the-vector-borne-disease-transmission-potential-in-north.

Paul KK, Dhar-Chowdhury P, Haque CE, Al-Amin HM, Goswami DR, Kafi MAH, Drebot MA, Lindsay LR, Ahsan GU, Brooks WA. Risk factors for the presence of dengue vector mosquitoes, and determinants of their prevalence and larval site selection in Dhaka, Bangladesh. PLoS One. 2018. 13(6): e0199457. doi:10.1371/journal.pone.0199457.

R Core Team. 2022. R: A language and environment for statistical computing. Vienna, Austria. URL https://www.R-project.org/.

Rahman KM, Sharker Y, Rumi RA, Khan M-UI, Shomik MS, Rahman MW, Billah SM, Rahman M, Streatfield PK, Harley D, Luby SP . An Association between Rainy Days with Clinical Dengue Fever in Dhaka, Bangladesh: Findings from a Hospital Based Study. Int J Environ Res Public Health. 2020. 17(24):9506. doi:10.3390/ijerph17249506.

Salje H, Morales I, Gurley ES, Saha S. Seasonal Distribution and Climatic Correlates of Dengue Disease in Dhaka, Bangladesh. Am J Trop Med Hyg. 2016. 94(6):1359–1361. doi:10.4269/ajtmh.15-0846.

Salje H, Paul KK, Paul R, Rodriguez-Barraquer I, Rahman Z, Alam MS, Rahman M, Al-Amin HM, Heffelfinger J, Gurley E. Nationally-representative serostudy of dengue in Bangladesh allows generalizable disease burden estimates. Elife. 2019. 8. doi:10.7554/eLife.42869.

Sen PK. Estimates of the Regression Coefficient Based on Kendall’s Tau. J Am Stat Assoc. 63(324):1379–1389. doi:10.1080/01621459.1968.10480934. d

Sharmin S, Glass K, Viennet E, Harley D. Geostatistical mapping of the seasonal spread of under-reported dengue cases in Bangladesh. PLoS Negl Trop Dis. 2018. 12(11):e0006947. doi:10.1371/journal.pntd.0006947.

Sharmin S, Viennet E, Glass K, Harley D. The emergence of dengue in Bangladesh: epidemiology, challenges and future disease risk. Trans R Soc Trop Med Hyg. 2015. 109(10):619–627. doi:10.1093/TRSTMH/TRV067.

Simmonds P, Becher P, Bukh J, Gould EA, Meyers G, Monath T, Muerhoff S, Pletnev A, Rico-Hesse R, Smith DB, Stapleton JT, Consortium ICTV ICTV Virus Taxonomy Profile: Flaviviridae. J Gen Virol. 2017. 98(1):2–3. doi:10.1099/jgv.0.000672.

Soneja S, Tsarouchi G, Lumbroso D, Tung DK. A Review of Dengue’s Historical and Future Health Risk from a Changing Climate. Curr Environ Health Rep. 2021. 8(3):245–265. doi:10.1007/s40572-021-00322-8.

Sumi SN, Sinha NC, Islam MA. Generalized linear models for analyzing count data of rainfall occurrences. SN Appl Sci. 2021.3(4):481. doi:10.1007/s42452-021-04467-x.

Tawsia Tajmim. Aedes larva density high in Gulshan, Banani, Motijheel, Gopibagh. The Business Standard. 2022. Dhaka:1–2.

Teo A, Tan HD, Loy T, Chia PY, Chua CLL. Understanding antibody-dependent enhancement in dengue: Are afucosylated IgG1s a concern? PLoS Pathog. 2023. 19(3):e1011223. doi:10.1371/journal.ppat.1011223.

Wang TT, Sewatanon J, Memoli MJ, Wrammert J, Bournazos S, Bhaumik SK, Pinsky BA, Chokephaibulkit K, Onlamoon N, Pattanapanyasat K, Taubenberger JK, Ahmed R, Ravetch JV: IgG antibodies to dengue enhanced for FcγRIIIA binding determine disease severity. Science 2017. 355(6323):395–398. doi:10.1126/science.aai8128.

Wangdi K, Clements ACA, Du T, Nery SV. Spatial and temporal patterns of dengue infections in Timor-Leste, 2005–2013. Parasit Vectors. 2018. 11(1):9. doi:10.1186/s13071-017-2588-4.

WHO. 2009. Dengue: Guidelines for diagnosis , treatment , prevention and control . Geneva, Switzerland. Pp 1-144.

WHO. 2023. Dengue and severe dengue. [accessed 2023 May 15]. https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue.

WHO South-East Asia. 2023. Dengue in South-East Asia. WHO Regional office for South-East Asia.:1–6.

WHO-Bangladesh. 2022. Dengue - Bangladesh. https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON424.

Yuan H-Y, Liang J, Lin P-S, Sucipto K, Tsegaye MM, Wen T-H, Pfeiffer S, Pfeiffer D. The effects of seasonal climate variability on dengue annual incidence in Hong Kong: A modelling study. Sci Rep. 2020. 10(1):4297. doi:10.1038/s41598-020-60309-7.

Yue S, Pilon P. A comparison of the power of the t test, Mann-Kendall and bootstrap tests for trend detection / Une comparaison de la puissance des tests t de Student, de Mann-Kendall et du bootstrap pour la détection de tendance. Hydrological Sciences Journal. 2004. 49(1):21–37. doi:10.1623/hysj.49.1.21.53996.

Tables and Figure Legends:

Tables:

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

Figures:

Fig 1A: Number of dengue cases and deaths over the period 2000-2022, Bangladesh. **1B:** Number of monthly dengue cases and deaths recorded in Bangladesh, 2000-2022.

Fig 2: The boxplot compares monthly rainfall in Dhaka city, Bangladesh between two decades (2000-2010 vs 2011-2022). The bottom and top of the box indicate the first and third quantiles, the band inside the box is the median. The dots outside the box are individual outliers. Most of the months in the second decade had outlier rainfall whereas in the first decade, only the cooler months (Nov-Jan) had some extreme rainfall.

Fig 3: Top: Mean monthly growth factor for the period of 2000-2022. **Bottom:** The Monthly growth factor for the individual year 2000-2022. The horizontal dashed line indicates monthly growth factor 1 (the same number of dengue cases in two subsequent months).

Fig 4: The observed and forecasted number of dengue cases in Bangladesh using the autoregressive moving average (ARIMA) model including a 95% confidence interval.

Two Decades of Endemic Dengue in Bangladesh (2000-2022): Trends, Seasonality, and Impact of Temperature and Rainfall Patterns on Transmission Dynamics

Mohammad Nayeem Hasan[1], Ibrahim Khalil [2], Muhammad Abdul Baker Chowdhury [3], Mahbubur Rahman [4,5], Md Asaduzzaman [6], Masum Billah [6], Laila An~~r~~juman Banu [7], Mahbub-ul Alam[8], Atik Ahsan [8], Tieble Traore [9], Md. Jamal Uddin[1,10] Roberto Galizi [11], Ilaria Russo[12], Alimuddin Zumla[13], Najmul Haider[11*]

[1] Department of Statistics, Shahjalal University of Science and Technology, Sylhet 3114, Bangladesh (MNH: nayeem5847@gmail.com, MJU: jamal-sta@sust.edu)

[2] Department of Livestock Services, Ministry of Fisheries and Livestock, Bangladesh, Dhaka, Bangladesh (IK: dribrahim.dls@gmail.com)

[3] Department of Neurosurgery, University of Florida College of Medicine, Gainesville, Florida FL 32610, USA (MABC: baker.chowdhury@neurosurgery.ufl.edu)

[4] The Royal Veterinary College, University of London, Hawkshead Lane, North Mymms, Hatfield, Hertfordshire, United Kingdom (Email: MR: dr_mahbub@yahoo.com)

[5] Institute of Epidemiology, Disease Control and Research (IEDCR), Ministry of Health and Family Welfare, Mohakhali, Dhaka, Bangladesh (MR: dr_mahbub@yahoo.com)

[6] School of Digital, Technologies, and Arts, Staffordshire University, Staffordshire, UK (MB: masum.billah@staffs.ac.uk , MA: Md.Asaduzzaman@staffs.ac.uk)

[7] Department of Anatomy, Bangabandhu Sheik Mujib Medical University, Dhaka, Bangladesh (dr.lailabanu@gmail.com)

[8] Environmental Intervention Unit, International Centre for Diarrhoeal Diseases Research, Bangladesh (ICDDR,B), Dhaka-1212, Bangladesh (MUA: mahbubalam@icddrb.org, AA: atik.ahsan@icddrb.org)

[9] Emergency Preparedness and Response Programme, WHO Regional Office for Africa, Dakar Hub, Daker, Senegal (TT: traoret@who.int)

[10] Department of General Educational and Development, Daffodil International University, Dhaka, Bangladesh (MJU: jamal-sta@sust.edu)

[11] School of Life Sciences, Faculty of Natural Sciences, Keele University, Keele, Staffordshire, United Kingdom, ST5 5BG (NH: n.haider@keele.ac.uk, RG: r.galizi@keele.ac.uk).

[12] School of Medicine, Faculty of Medicine and Health Sciences, Keele University, Staffordshire, ST5 5BG, United Kingdom (IR: i.russo@keele.ac.uk)

[13] Division of Infection and Immunity, Centre for Clinical Microbiology, University College London and NIHR-BRC, University College London Hospitals, London, United Kingdom (AZ: a.zumla@ucl.ac.uk).

***Corresponding author (NH):** Dr Najmul Haider, School of Life Sciences, Keele University, Huxley Building, Room 122, Keele, Staffordshire, ST5 5BG, United Kingdom, Email: n.haider@keele.ac.uk , Phone : **(+44) 01782 734414**

Abstract:

Background: The objectives of this study were to compare dengue virus (DENV) cases, deaths, case-fatality ratio, and meteorological parameters between the first and the recent decade of this century (2000-2010 vs. 2011-2022) and to describe the trends, seasonality, and impact of change of temperature and rainfall patterns on transmission dynamics of dengue in Bangladesh

Methods: For the period 2000-2022, dengue cases and death data from Bangladesh's Ministry of Health and Family Welfare's website, and meteorological data from the Bangladesh Meteorological Department were analyzed. A Poisson regression model was performed to identify the impact of meteorological parameters on the monthly dengue cases. A forecast of dengue cases was performed using an autoregressive integrated moving average model.

Results: Over the past 22 years, a total of 244,246 dengue cases were reported including 849 deaths (Case fatality ratio [CFR] =0.34%). The mean annual number of dengue cases increased eight times during the second decade, with 2,216 cases during 2000-2010 vs. 18,321 cases during 2011-2022. The mean annual number of deaths doubled (21 vs. 46), but the overall CFR has decreased by one-third (0.69% vs 0.23%). Concurrently, the annual mean temperature increased by 0.49 °C, and rainfall decreased by 314 mm with altered precipitation seasonality. Monthly mean temperature (Incidence risk ratio [IRR]: 1.26), first-lagged rainfall (IRR: 1.08), and second-lagged rainfall (IRR: 1.17) were significantly associated with monthly dengue cases.

Conclusions: The increased local temperature and changes in rainfall seasonality might have contributed to the increased dengue cases in Bangladesh.

Keywords: Dengue, Bangladesh, Climate change, Temperature, Rainfall

Introduction:

Dengue fever is a mosquito-borne disease (MVD) caused by four distinct serotypes of the dengue virus (DENV) within the family *Flaviviridae* (Simmonds et al. 2017). DENV is transmitted to humans by bites of *Aedes aegypti* (L.) and *Aedes albopictus* (Skuse) (WHO 2009; CDC 2019). DENV is endemic in over 125 countries, and the number of cases globally reported to WHO continues to increase yearly (Bhatt et al. 2013; WHO 2023). Annually, an estimated 390 million dengue infections are estimated worldwide, including 96 million clinical cases making DENV one of the most important vector-borne diseases (VBDs) (Murray et al. 2013; Messina et al. 2019; WHO 2023). Most infections (>80%) are self-limiting with no or mild clinical manifestation resulting in lifelong immunity for that serotype (WHO-Bangladesh 2022). However, reinfection with different serotypes, known as secondary or tertiary dengue infection, may result in severe dengue with an increasing risk of fatal outcome (Teo et al. 2023).

Currently, South and Southeast Asia are ‘hotspots’ of DENV infection, with more than 50% of cases recorded in these regions (WHO South-East Asia 2023). The first DENV 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). Over the past few years, the number of dengue cases has been steadily increasing, with significant seasonal and regional variation. Analysis of data from 2000 to 2017 revealed that almost half of the dengue cases occurred during the monsoon (May-August) and the post-monsoon (September-December) seasons (Mutsuddy et al. 2019). Historically the monsoon has been the primary dengue transmission season in Bangladesh, although the number of dengue cases has increased during the post-monsoon season in recent years (Haider et al. 2021; Hossain et al. 2023).

Bangladesh’s hot and humid weather favors the production of a large variety of mosquito species with more than 123 species listed in 2016 (Irish et al. 2016; Bashar et al. 2016). The most common vectors of dengue virus, *Ae aegypti* and *Ae albopictus,* were first recorded in 1952 (Asir-Ud-Din M 1952) and recent studies in Dhaka showed a higher Breteau index which measures the number of positive containers per 100 households: 30.8 in 1997, 24.6 in 2000, 55.8 in 2011, 28.7 in 2012 and 22.5 in 2013 (Ferdousi et al. 2015; Paul et al. 2018). In 2022, the maximum Breteau index of >50 was recorded for six wards of the Dhaka South City Corporation area (Tawsia Tajmim 2022). The pupal index (PI) which measures the number of pupae per 100 houses was estimated during the monsoon season in several years in Bangladesh: 62.2 in 2011, 153.5 in 2012, and 75.9 in 2013. However, during the dry period, the PI was estimated as 16.7 in 2012 (Paul et al. 2018).

Climate change, including changes in precipitation, temperature and humidity, as well as rapid unplanned urbanization, were identified as strong indicators of an ecological imbalance that has led to an increase in dengue cases in Bangladesh (Mutsuddy et al. 2019). These changes could eventually extend dengue transmission season year-round, with a chance of outbreaks occurring at any time of the year. Identifying trends and seasonality in dengue cases may aid health authorities and relevant public and private administrations in effectively allocating resources to control the spread of the DENV through vector control. The objectives of our current study were to: i) compare the annual and monthly number of dengue cases and deaths between 2000 and 2022, ii) identify the overall trend and seasonality of dengue cases, iii) quantify the impact of weather parameters on the number of monthly dengue cases, and iv) forecast the annual number of dengue cases for the next decade.

Methods:

Data sources:

The current dengue surveillance in Bangladesh is coordinated by the Management Information System (MIS) of the Ministry of Health and Family Welfare of Bangladesh (Haider et al. 2023 Sep). The surveillance includes hospitalized patients diagnosed as infected with dengue virus primarily from government hospitals except in the capital city Dhaka, where more than 57 private hospitals are included in addition to 20 public hospitals. Outside the capital city Dhaka, the central district hospital of 64 districts and medical college hospitals are also included in the surveillance system. We collected data on the number of reported dengue cases and deaths from the publicly shared database of the MIS from January 2000 to December 2022. The Ministry of Health and Family Welfare, Bangladesh defines dengue cases based on clinical symptoms (including fever and rash) and/or laboratory tests for IgM or IgG antibodies to DENV and nonstructural 1 protein (NS-1) of DENV (Ahsan et al. 2021).

We used three-hourly temperature and daily rainfall data from the Bangladesh Meteorological Department (BMD) over the period 2000–2022 from the meteorological station located in Mirpur, Dhaka (Lat 23.46, Lon 90.23). Given Bangladesh's relatively small land size and moderate climate variation across the country, we focused data solely on the Dhaka station. Furthermore, a substantial proportion of historical dengue cases (>90%) have originated from Dhaka city (Sharmin et al. 2018).

Procedures

The monthly number of reported dengue cases was used as the primary outcome variable. Two weather variables, temperature, and rainfall were used as the covariates for the regression analysis. In addition, monthly rainfall lagged by 1 or 2 preceding months was also used as predictors for the number of monthly dengue cases.

Statistical analysis

We analyzed the monthly dengue cases and meteorological data for the period of 2000-2022. We used 2010 (the median year) to divide the period 2000-2022. Then, we compared the number of dengue cases, deaths, and weather parameters during the two decades (2000-2010 and 2011-2022) using a paired sample t-test, aimed at comparing trends, developments, and changes between these periods. In the first stage, descriptive analyses were conducted to determine the characteristics of dengue cases and deaths, with mean~~,~~ and interquartile range (IQR) in each year and each month calculated for the entire period. Next, we calculated the monthly growth factor (GF) of dengue cases by dividing the number of dengue cases reported in each month by the number of dengue cases reported in the previous month and repeating this process for each month from 2000 to 2022 (Haider et al. 2021). The formula for the growth factor can be given by

$$GF_t = \frac{N_{t+1} + 1}{N_t + 1}$$

where N_t indicates the number of dengue cases in t^{th} month. To avoid the occurrence of zeros in some months, we added 1 to the total number of cases for each month. The distribution of the GF was skewed; therefore, we used the natural log transformation before the data was further examined. However, we have also performed a reverse transformation of the log (GF) values by back-transforming ~~exponentiating~~ values to the original scale for ease of interpretation (Haider et al. 2021). A monthly GF greater than 1 indicates that the number of dengue cases would be more than the number of dengue cases of the previous month, while a GF less than 1 means that the number of dengue cases in a new month would be less than the previous month. For example, if there are 100 cases in January, the number of dengue cases in February would be 200 when the value of GF is 2.0 or 50 cases when the value of GF is 0.5 in January (Haider et al. 2021)

We performed forecasting using the autoregressive integrated moving average (ARIMA) model. The ARIMA model is a data-driven, exploratory strategy that enabled us to fit a suitable model and forecast values. The ARIMA model consists of autoregressive (p) terms, differencing (d) terms, and moving average (q) operations, and it is denoted as ARIMA (p, d, q) (Kumar and Susan 2020). To select the appropriate autoregressive and moving average orders, the autocorrelation function (ACF) and partial autocorrelation function (PACF) were examined. Additionally, the differencing parameter, represented by "d," indicated the number of times the time series was different to achieve stationarity (Hasan et al. 2021). 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 possible upward or downward trends (Yue and Pilon 2004). The null hypothesis posits no monotonic trend, while the alternative hypothesis suggests the presence of a trend, which could be positive, negative, or non-null. We also performed Sen's slope test to assess variations in annual dengue cases and deaths. The slope greater than 0 indicates an upward trend and less than 0 indicates a downward trend of a given period (Sen 1968).

We then used a time series count generalized linear model (GLM), more specifically, a time-series Poisson regression model, to determine whether the meteorological factors were associated with the change in dengue cases over time (Sumi et al. 2021). Monthly dengue cases were utilized as the outcome variable in this ~~model, along withpredicted~~model predicted by temperature and rainfall data from the Bangladesh Meteorological Department (BMD)~~ on temperature and rainfall~~. We have estimated the degree-hour of heat generated by the addition~~al~~ temperature each year in Bangladesh. To compare this with the extrinsic incubation period (EIP) of the dengue virus in *Aedes* mosquito, we estimated the degree-hour required to complete the extrinsic incubation period (EIP) at 26° C using the mathematical formula [-0.1393 + 0.008*Temp] presented by Focks et al. (1995). ~~(Focks et al. 1995).~~ We used the statistical program RStudio, version 3.5.2.2 for the analyses (R Core Team 2022).

Results:

Between 2000 and 2022, DGHS reported a total of 244,246 dengue cases, with an annual mean of 10,619 cases (interquartile range [IQR]: 859.5-5,805.5), including 849 fatal outcomes with a case-fatality ratio (CFR) of 0.34%. Between 2000 to 2010, the mean annual number of dengue cases was 2,216 (IQR: 480-3182) which increased by 8 times in the following decade (2011-2022) at 18,321 (IQR: 1405-28429, p=0.22) **(Table 1)**. Between these two periods, the mean number of annual deaths due to DENV cases increased by 2.2 times, from 21.2 to 46.6 cases (p=0.85). However, the CFR of DENV cases decreased slightly from 0.69% to 0.23% (p=0.08) (**Table 1)**.

The highest monthly average number of cases was recorded in August (n=3,407 cases) and the lowest was in March (n=6.7 cases) **(Fig 1B)**. The highest number of annual cases was reported in 2019 with 101,354. The highest number of deaths was recorded in 2022 with 281 deaths, which was 35% of total deaths recorded in the past 23 years in Bangladesh **(Fig 1)**. Most (65%, n=550) ~~of the~~ dengue-related deaths were recorded after 2018 **(Fig 1)**.

The average annual temperature was 26.35 °C (SD=0.49) during the first decade (2000-2010) and 26.84 °C (SD=0.37) during the recent decade (2011-2022) (**Table 1**). The increase of 0.49° C temperature was equivalent to 4,292 degree-hours/year of heat (365 days X 24 hours X 0.49° C). For dengue virus transmission, approximately 349-degree-hours of equivalent heat is needed to complete the EIP of DENV in the *Aedes* mosquito at 26° C (Focks et al. 1995). The annual total rainfall decreased by 314 mm between the two decades, from 2078.6 mm to 1764.5 mm (**Table 1**), of which 308 mm decreased during the monsoon (July-October) season and only 6 mm decreased during the non-monsoon period. However, during pre-and-post monsoon season, rainfall (more than 3rd quantile value of monthly rainfall for the decade) increased in the second decade **(Fig 2)**.

The overall mean GF for the number of dengue cases per 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 for 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. June had the highest GF with a mean value of 3.47 indicating that cases would be more than 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 nearly halved compared to the number of cases recorded in December (**Fig. 3**).

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) with a tau value of 0.26 and p-value of 0.14 indicating a non-significant upward trend ~~in upcoming months~~.

In the GLM, the estimated effect of each variable is presented as the incidence risk ratio (IRR). The model indicates that dengue cases would rise by 26% with a one-degree centigrade (°C) temperature increase. 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: 1.08-1.09]), and in the second lagged month increases in cases would be by 17% [IRR=1. 17 (95% CI: 1. 17 -1.18)].

In the ARIMA model, we detected an increasing trend for the first few years, which then started to decline. However, a strong rise in cases was observed after 2018 except for 2020 (the first year of the COVID-19 pandemic). The forecasted value showed a flat line with reduced variation over time in the number of dengue cases in Bangladesh **(Fig 4)**.

Discussion:

Dengue is currently an important public health challenge for Bangladesh. Our analysis showed that the number of DENV cases has increased eight times, deaths have doubled, and the CFR dropped to one-third between the first and second decades of this century. Between these periods, the annual temperature increased by 0.49°C, and annual rainfall decreased by 314 mm, despite changes in the seasonality of rainfall with unusually early or late rainfall outside the typical monsoon season (July-October) (Haider et al. 2014). The monthly growth factor remained above one for four months (April to July) which overlapped the hot and humid period of the year. Monthly mean temperature, monthly first-lagged rainfall, and second-lagged rainfall played a critical role in monthly dengue cases in Bangladesh.

The average increase of 0.49°C temperature added approximately 4,292-degree-hours of equivalent heat per year. This additional heat would favor vector borne disease (VBD) transmission. For DENV, approximately 349-degree-hours equivalent heat is needed to complete the EIP in *Aedes* mosquitoes at 26° C (Focks et al. 1995). Therefore, the addition of 0.49°C temperature shortens the duration of the EIP and thus increases the rate of virus dengue transmission. ~~.~~ An 8-fold increase in dengue cases is a possible indication of the impact of increases in temperature in the country. Our model identified a significant role of monthly mean temperature, with an additional 1°C temperature increasing the monthly cases by 26%. Earlier studies showed that for every 1°C increase in temperature, dengue cases increased by 61% in Australia, 12-22% in Cambodia, 5% in Vietnam, and 2.6% in Mexico (Soneja et al. 2021). Increasing temperatures can accelerate mosquito population growth and shorten the duration of the EIP of the virus, thereby allowing an increased the biting rate and more frequent transmission (Najmul Haider 2018; Couper et al. 2021). Decreased rainfall can increase the risk of dengue, especially in urbanized areas that may have an inadequate and intermittent water supply during drought (Lowe et al. 2021).

Rainfall provides oviposition and larval developmental sites and thereby plays an important role in mosquito population size and pathogen transmission. Although we found a 15% reduction in annual rainfall in the recent decade from the immediate past decade, we detected an increase in rainfall during pre-and-post monsoon seasons, thereby extending the season for mosquitoes and other arthropod vectors. Our model showed that the first and second lagged month's rainfall increased monthly cases by 8% and 17%, respectively. These findings were consistent with earlier studies in Bangladesh that showed that peak dengue cases occurred two months after peak rainfall (Salje et al. 2016) or an additional rainy day per month increased dengue cases by 6% in the succeeding month (Rahman et al. 2020). Similar findings were reported in Vietnam with dengue cases being associated with both first and second-lagged months (Cuong et al. 2011). In the greater part of the capital city Dhaka, there is a shortage of ~~regular supply of~~municipal water, and thus people attempt to store municipal water when available as well as rainwater. This might facilitate the production of *Aedes* mosquitoes (Akanda et al. 2020). In Timor-Leste, a 47% increase in dengue cases was recorded with an additional 1 mm seasonal rainfall increase (Wangdi et al. 2018). These findings are biologically plausible as altered precipitation during pre- and post-monsoon allows extended vector seasons facilitating additional human cases (Yuan et al. 2020).

Bangladesh's dengue season is characterized by hot and wet periods from~~between~~ June to August. This is the period with the highest amount of rainfall facilitating *Aedes* abundance (Haider et al. 2023 May 18). The monthly mean growth factor above 1 for April – June indicates that for each of these months, the number of dengue cases will surpass the previous month. Thus, we suggest starting vector control intervention in April in Bangladesh.

Two large dengue outbreaks occurred in Bangladesh in 2019 and 2022, with both characterized by unusual weather patterns and the occurrence of two different DENV serotypes. The 2019 outbreak was characterized by early rainfall of 120 mm in February compared to a historical monthly mean of 20 mm precipitation, along with the introduction DENV-3 (Ahsan et al. 2021). The 2022 outbreak was characterized by the late onset of rainfall, with 297 mm of rainfall in October compared to a monthly mean of 156 mm that may have prolonged the vector transmission season and by the introduction of DENV-4 (Haider et al. 2023 May 18). The introduction this new serotype exposed a largely naïve population in a densely populated country like Bangladesh. A large proportion of the population had already been infected with one or more serotypes of DENV with more than 80% of people living in Dhaka having antibodies against DENV (Salje et al. 2016). Another study predicted an estimated 40 million people had been infected with DENV nationally, with 2.4 million annual infections (Salje et al. 2019). Thus, any subsequent infections raise the risk of developing severe dengue hemorrhagic fever through antibody-dependent enhancement (ADE) (Teo et al. 2023). The deaths of many people in 2022 when DENV-4 was introduced were probably associated with secondary and/or tertiary DENV infection (Haider et al. 2023 May 18).

Our analysis shows that there was a significant monotonic increasing trend of dengue cases in Bangladesh for the period 2000-2022 (M-K trend test);~~,~~ however, the magnitude of the increasing trend was not significant (Sen's Slope test). This might be due to the large variation of the cases reported in different years. For example, more than 82% of dengue cases (n=202,425) that were recorded in the last 23 years (2000-2023) were reported in the recent five years (2018-2022). The~~is~~ increase in case reporting in recent years might be a true increase in dengue cases or could be the result of the development of the health care system, improved diagnostic system, and inclusion of more hospitals in the surveillance system in Bangladesh (Haider et al. 2023 Sep).

Controlling vector-borne diseases in tropical countries where temperatures, humidity, and rainfall remain favorable for mosquitoes during most of the year is a difficult task (Haider et al. 2023 May 18). Concerns have been raised over the development of insecticide resistance (Al-Amin et al. 2020; Ahsan et al. 2021) and the failure of developing a successful dengue vaccine (Wang et al. 2017). The prospect of *Wolbachia*-related intervention is still far from being applied on a national scale considering the expenses and associated technicalities. In this situation, an integrated and holistic vector management plan~~-~~ engaging the local communities is key for controlling *Aedes*-borne diseases, especially in resource-limited countries. Regular destruction of mosquito developmental sites and increasing surveillance for detecting active cases are key to limiting dengue virus infections. The development of a municipal water system that would preclude the need to store water is ~~-~~essential to prevent *Aedes* mosquito production. Continuous active surveillance for DENV cases will enable early detection of cases and the location of outbreaks. Public health authorities will be able to identify areas where the disease is spreading, take immediate action to control mosquito populations, isolate infected patients, and implement public awareness campaigns to educate people about preventive measures. Early detection and response can help prevent the further spread of the disease and reduce its impact.

Several weaknesses may have impacted our study. We relied on the reported number of cases from the Ministry of Health and Family Welfare's website, which mainly relies on passive reporting systems from the selected health facilities in the country (Ahsan et al. 2021). These numbers seem to underestimate the actual number of infections and fever cases. The hospitals included in the surveillance system are only a small fraction of total healthcare facilities in Bangladesh (~5%) where dengue patients can seek healthcare (Haider et al. 2023 Sep). A modeling study based on the national seroprevalence of DENV antibodies predicted an annual infection of 2.4 million people (Salje et al. 2019). Dengue cases similarly are underestimated globally as it is difficult to detect asymptomatic or mild cases that never reach healthcare settings. Although mild cases are missed frequently, ~~the~~ severe and fatal cases would likely visit the hospital and thus be counted as numerators in our estimates. Thus, our estimation did not overlook the worst-case scenario, but may have estimated a higher CFR because of the underestimation of the denominators. Another limitation pertains to our exclusive utilization of weather data from the Dhaka station. Given Bangladesh's relatively small size and the moderate climate variation across the country, we focused our data collection solely on the Dhaka station. Furthermore, a substantial proportion of historical dengue data originates from Dhaka city. We could not use herd immunity data in our model as these data are not available for different serotypes of DENV in Bangladesh. However, earlier studies show that people living in the capital city and larger cities like Chittagong have higher seroprevalence compared to rural areas where the seroprevalence was as low as 3% (Salje et al. 2019). This also illustrates a high risk of antibody-dependent enhancement (ADE) through secondary and tertiary infection in large cities. We accept that the increase in dengue cases in the recent decade could be a result of multiple factors that we could not include in the analysis. These factors include the improvement of the healthcare system which now detects a greater proportion of clinical cases than in the past, the arrival of new serotypes of DENV, and the increased size of the urban population.

Conclusions:

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 may partly be explained by global warming, with an increase of 0.49°C annual temperature as well as changes in duration and length of the rainy season. Unusual early or late rain in and beyond the monsoon season likely contributed to extending the length of the dengue transmission season in Bangladesh. The monthly mean temperature and monthly total rainfall of the first-lagged month and second-lagged months showed a large influence on the monthly DENV cases in Bangladesh. The mean monthly growth factor remained significantly above one during April-July, which coincided with the hot and rainy season of the country indicating an earlier vector control would benefit the country. ~~The ARIMA model forecasted a continuously increasing trend of DENV cases for the next decade in Bangladesh~~. We recommend an integrated and holistic vector management plan ~~while~~ engaging ~~the~~ local communities in the elimination of mosquito larval habitats and increasing surveillance for detecting active dengue

Commented [wkr1]: This does not agree with Fig 4 or the corresponding section of your Reseults section.

Commented [NH2R2]: Agree and deleted this statement.

cases. Proactive surveillance, vector control, and community engagement ~~vaccine rollout~~ remain essential public health interventions. In the context of climate change, urbanization, trade, and the movement of infected people, there is a need to operationalize the One Health approach to address dengue fever and other vector-borne diseases in Bangladesh and beyond.

Commented [wkr3]: Above you indicate this is not planned in the immediate future?

Commented [NH4R4]: Deleted the word. However, we added the phrase 'community engagement'

Acknowledgments:

We are grateful to the Ministry of Health and Family Welfare of Bangladesh for publicly sharing the dengue cases and deaths data. We acknowledge the Bangladesh Meteorological Department for sharing the meteorological data. NH, and AZ, are part of the PANDORA-ID-NET Consortium (EDCTP 373 Reg/Grant RIA2016E-1609) funded by the European and Developing Countries Clinical Trials Partnership (EDCTP2) program. NH is a member of the International Development Research Centre, Canada's grant on West African One Health Actions for understanding, preventing, and mitigating outbreaks (109810-001). AZ is a National Institutes of Health Research senior investigator, and a Mahathir Science Award and Pascoal Mocumbi Award laureate.

Author contribution statement: NH ideated the study and all authors helped develop the study outline and protocol. MNH and IK collected the data. NH, MNH, MA and AZ analyzed the data. NH, IK and MNH prepared the first draft manuscript and all authors contributed to several drafts and finalization of the manuscript. All authors approved the final draft and submission of the manuscript.

Financial Support: There was no funding for this research.

Conflict of interest: The authors declare that they have no conflict of interest.

Ethics statement: This study does not include individual-level data and thus does not require ethical approval. We used publicly available data on Dengue cases and deaths.

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/).

References

Ahsan A, Haider N, Kock R, Benfield C. ~~2021.~~ Possible Drivers of the 2019 Dengue Outbreak in Bangladesh: The n~~N~~eed for a r~~R~~obust c~~C~~ommunity-l~~L~~evel s~~S~~urveillance s~~S~~ystem. ~~Reisen W, editor.~~ J Med Entomol,~~.~~ 2021: 58(1):37–39. doi:10.1093/jme/tjaa150. ~~https://academic.oup.com/jme/advance-article/doi/10.1093/jme/tjaa150/5877896.~~

Akanda AS, Johnson K, Ginsberg HS, Couret J. ~~2020.~~ Prioritizing w~~W~~ater s~~S~~ecurity in the m~~M~~anagement of v~~V~~ector-b~~B~~orne d~~D~~iseases: Lessons f~~F~~rom Oaxaca, Mexico. Geohealth, ~~.~~2020: 4(3). doi:10.1029/2019GH000201.

Al-Amin HM, Johora FT, Irish SR, Hossainey MRH, Vizcaino L, Paul KK, Khan WA, Haque R, Alam MS, Lenhart A. ~~2020.~~ Insecticide resistance status of *Aedes aegypti* in Bangladesh. Parasit Vectors,~~.~~ 2020: 13(1):622. doi:10.1186/s13071-020-04503-6. ~~https://doi.org/10.1186/s13071-020-04503-6.~~

Asir-Ud-Din M. ~~1952.~~ Mosquitoes breeding in tree-holes and bamboo stumps in Dacca (East Pakistan). 1952:~~.~~ 2: 110–112. Pakistan Journal of Health. 2:110–112.

Bashar K, Rahman MdS, Nodi IJ, Howlader AJ. ~~2016.~~ Species composition and habitat characterization of mosquito (Diptera: Culicidae) larvae in semi-urban areas of Dhaka, Bangladesh. Pathog Glob Health. 2016:~~.~~ 110(2):48–61. doi:10.1080/20477724.2016.1179862.

Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, Drake JM, Brownstein JS, Hoen AG, Sankoh O, Myers MF, George DB, Jaenisch T, Wint GRW, Simmons CP, Scott TW, Farrar JJ, Hay SI. ~~et al.~~ ~~2013.~~ The global distribution and burden of dengue. Nature. 2013: 496(7446):504–7. doi:10.1038/nature12060. ~~http://www.ncbi.nlm.nih.gov/pubmed/23563266.~~

CDC. 2019. Transmission through mosquito bites. [accessed 2023 May 15]. https://www.cdc.gov/dengue/transmission/index.html.

Couper LI, Farner JE, Caldwell JM, Childs ML, Harris MJ, Kirk DG, Nova N, Shocket M, Skinner EB, Uricchio LH, Exposite-Alonso M, Mordecai EA. ~~et al. 2021.~~ How will mosquitoes adapt to climate warming? Elife. 2021:~~.~~ 10. doi:10.7554/eLife.69630.

Cuong HQ, Hien NT, Duong TN, Phong TV, Cam NN, Farrar J, Nam VS, Thai KTD, Horby P. 2011. Quantifying the Emergence of Dengue in Hanoi, Vietnam: 1998–2009. PLoS Negl Trop Dis. 5(9):e1322. doi:10.1371/journal.pntd.0001322.

Ferdousi F, Yoshimatsu S, Ma E, Sohel N, Wagatsuma Y. ~~2015.~~ Identification of Essential Containers for Aedes Larval Breeding to Control Dengue in Dhaka, Bangladesh. Trop Med Health. 2015:~~.~~ 43(4):253–64. doi:10.2149/tmh.2015-16.

Focks DA, Daniels E, Haile DG, Keesling JE. ~~1995.~~ A simulation model of the epidemiology of urban dengue fever: Literature analysis, model development, preliminary validation, and samples of simulation results. Am~~erican~~ J~~ournal~~ of Trop~~ical~~ Med~~icine~~ and Hyg~~iene~~. 1995:~~.~~ doi:10.4269/ajtmh.1995.53.489.

Commented [wkr5]: Thank you for improving your Reference Section ; however, your format does NOT agree exactly. Please see the changes I have made, some of which you will have to manually change to your reference data base. Please see the guide I linked previously and a recent issue of JME. Please note: THESE ARE THE SAME EDITS MADE PREVIOUSLY.

Commented [wkr6]: Include all authors

Commented [NH7R7]: Included ..

Haider N, Asaduzzaman M, Hassan MN, Rahman M, Sharif AR, Ashrafi SAA, Lee SS, Zumla A. 2023 Sep. Bangladesh's 2023 Dengue outbreak – age/gender-related disparity in morbidity and mortality and geographic variability of epidemic burdens. Int.~~ernational~~ J.~~ournal of~~ Inf.~~ectious~~ Dis.~~eases~~. 2023. doi:10.1016/j.ijid.2023.08.026.

Haider N, Chang Y-M, Rahman M, Zumla A, Kock RA. 2021. 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. Current Res.~~earch~~ in Parasitol.~~ogy &~~ Vector-Borne Dis.~~eases.~~ 1:100063. doi:10.1016/j.crpvbd.2021.100063.

Haider N, Hasan MN, Khalil I, Tonge D, Hegde S, Chowdhury MAB, Rahman M, Hossain Khan M, Ansumana R, Zumla A, Uddin MJ ~~et al. 2023 May 18~~. The 2022 dengue outbreak in Bangladesh: hypotheses for the late resurgence of cases and fatalities. J Med Entomol. 2023. doi:10.1093/jme/tjad057.

Haider N, Rahman MS, Khan SU, Mikolon A, Gurley ES, Osmani MG, Shanta IS, Paul SK, Macfarlane-Berry L, Islam A, Desmon J, Epstein JH, Daszak P. Azim T. Luby SP, Zeidner NZ, Rahman MZ. ~~et al. 2014~~. Identification and Epidemiology of a Rare HoBi-Like Pestivirus Strain in Bangladesh. Transbound Emerg Dis. 2014. 61(3):193–198. doi:10.1111/tbed.12218. ~~http://doi.wiley.com/10.1111/tbed.12218~~.

Hasan MN, Haider N, Stigler FL, Khan RA, McCoy D, Zumla A, Kock RA, Uddin MJ. ~~2021.~~ The Global Case-Fatality Rate of COVID-19 Has Been Declining Since May 2020. Am J Trop Med Hyg. 2021.104(6):2176–2184. doi:10.4269/ajtmh.20-1496. ~~http://www.ncbi.nlm.nih.gov/pubmed/33882025.~~

Hossain MS, Noman A Al, Mamun SA Al, Mosabbir A Al. ~~2023.~~ Twenty-two years of dengue outbreaks in Bangladesh: epidemiology, clinical spectrum, serotypes, and future disease risks. Trop Med Health. 2023. 51(1):37. doi:10.1186/s41182-023-00528-6.

Irish SR, Al-Amin HM, Alam MS, Harbach RE. ~~2016.~~ A review of the mosquito species (Diptera: Culicidae) of Bangladesh. Parasit Vectors. 2016. 9(1):559. doi:10.1186/s13071-016-1848-z.

Kumar N, Susan S. 2020. COVID-19 Pandemic Prediction using Time Series Forecasting Models. In: ~~2020~~ 11th International Conference on Computing, Communication and Networking Technologies (ICCCNT). IEEE. 2020. p. 1–7.

Lowe R, Lee SA, O'Reilly KM, Brady OJ, Bastos L, Carrasco-Escobar G, de Castro Catão R, Colón-González FJ, Barcellos C, Carvalho MS, Blangiardo M, Rue H, Gasparrini A. ~~et al~~. ~~2021.~~ Combined effects of hydrometeorological hazards and urbanisation on dengue risk in Brazil: a spatiotemporal modelling study. Lancet Planet Health. 2021. 5(4):e209–e219. doi:10.1016/S2542-5196(20)30292-8.

Messina JP, Brady OJ, Golding N, Kraemer MUG, Wint GRW, Ray SE, Pigott DM, Shearer FM, Johnson K, Earl L, Marczak LB, Shirude S, Weaver ND, Gilbert M, Velayudhan R, Jones P, Jaenisch T, Scott TW, Reiner RC, Hay SI ~~et al~~. ~~2019.~~ The current and future global distribution and population at risk of dengue. Nat Microbiol. 2019. 4(9):1508–1515. doi:10.1038/s41564-019-0476-8.

Murray NEA, Quam MB, Wilder-Smith A. ~~2013.~~ Epidemiology of dengue: past, present and future prospects. Clin Epidemiol. 2013. 5(1):299–309. doi:10.2147/CLEP.S34440. ~~[accessed 2023 May 15]. https://pubmed.ncbi.nlm.nih.gov/23990732/.~~

Mutsuddy P, Tahmina Jhora S, Shamsuzzaman AKM, Kaisar SMG, Khan MNA, Dhiman S. ~~2019.~~ Dengue Situation in Bangladesh: An Epidemiological Shift in terms of Morbidity and Mortality. Can J Infect Dis Med Microbiol. 2019. doi:10.1155/2019/3516284. ~~[accessed 2023 May 15]. /pmc/articles/PMC6431455/.~~

Najmul Haider. ~~2018.~~ Modeling the vector-borne disease transmission potential in northern Europe with a special emphasis on microclimatic temperature: PhD Thesis. 2018. [Lyngby]: Technical University of Denmark. [accessed 2023 Nov 28]. https://orbit.dtu.dk/en/publications/modeling-the-vector-borne-disease-transmission-potential-in-north.

Paul KK, Dhar-Chowdhury P, Haque CE, Al-Amin HM, Goswami DR, Kafi MAH, Drebot MA, Lindsay LR, Ahsan GU, Brooks WA. ~~2018.~~ Risk factors for the presence of dengue vector mosquitoes, and determinants of their prevalence and larval site selection in Dhaka, Bangladesh. PLoS One. 2018. 13(6): e0199457. doi:10.1371/journal.pone.0199457.

R Core Team. 2022. R: A language and environment for statistical computing. Vienna, Austria. URL https://www.R-project.org/.

Rahman KM, Sharker Y, Rumi RA, Khan M-UI, Shomik MS, Rahman MW, Billah SM, Rahman M, Streatfield PK, Harley D, Luby SP ~~et al. 2020~~. An Association between Rainy Days with Clinical Dengue Fever in Dhaka, Bangladesh: Findings from a Hospital Based Study. Int J Environ Res Public Health. 2020. 17(24):9506. doi:10.3390/ijerph17249506.

Salje H, Morales I, Gurley ES, Saha S. ~~2016.~~ Seasonal Distribution and Climatic Correlates of Dengue Disease in Dhaka, Bangladesh. Am J Trop Med Hyg. 2016. 94(6):1359–1361. doi:10.4269/ajtmh.15-0846. ~~http://www.ajtmh.org/content/journals/10.4269/ajtmh.15-0846.~~

Salje H, Paul KK, Paul R, Rodriguez-Barraquer I, Rahman Z, Alam MS, Rahman M, Al-Amin HM, Heffelfinger J, Gurley E. ~~2019.~~ Nationally-representative serostudy of dengue in Bangladesh allows generalizable disease burden estimates. Elife. 2019. 8. doi:10.7554/eLife.42869.

Sen PK. ~~1968.~~ Estimates of the Regression Coefficient Based on Kendall's Tau. J Am Stat Assoc. 63(324):1379–1389. doi:10.1080/01621459.1968.10480934. ~~http://www.tandfonline.com/doi/abs/10.1080/01621459.1968.10480934.d~~

Sharmin S, Glass K, Viennet E, Harley D. ~~2018.~~ Geostatistical mapping of the seasonal spread of under-reported dengue cases in Bangladesh. ~~Barker CM, editor.~~ PLoS Negl Trop Dis. 2018. 12(11):e0006947. doi:10.1371/journal.pntd.0006947. ~~https://dx.plos.org/10.1371/journal.pntd.0006947.~~

Sharmin S, Viennet E, Glass K, Harley D. ~~2015.~~ The emergence of dengue in Bangladesh: epidemiology, challenges and future disease risk. Trans R Soc Trop Med Hyg. 2015. 109(10):619–627. doi:10.1093/TRSTMH/TRV067. ~~[accessed 2023 May 15]. https://pubmed.ncbi.nlm.nih.gov/26333430/.~~

Simmonds P, Becher P, Bukh J, Gould EA, Meyers G, Monath T, Muerhoff S, Pletnev A, Rico-Hesse R, Smith DB, Stapleton JT, Consortium ICTV ~~et al. 2017.~~ ICTV Virus Taxonomy Profile: Flaviviridae. J Gen Virol. 2017. 98(1):2–3. doi:10.1099/jgv.0.000672.

Soneja S, Tsarouchi G, Lumbroso D, Tung DK. ~~2021.~~ A Review of Dengue's Historical and Future Health Risk from a Changing Climate. Curr Environ Health Rep. 2021. 8(3):245–265. doi:10.1007/s40572-021-00322-8.

Sumi SN, Sinha NC, Islam MA. ~~2021.~~ Generalized linear models for analyzing count data of rainfall occurrences. SN Appl Sci. 2021.3(4):481. doi:10.1007/s42452-021-04467-x.

Tawsia Tajmim. ~~2022.~~ Aedes larva density high in Gulshan, Banani, Motijheel, Gopibagh. The Business Standard. 2022. Dhaka:1–2.

Teo A, Tan HD, Loy T, Chia PY, Chua CLL. ~~2023.~~ Understanding antibody-dependent enhancement in dengue: Are afucosylated IgG1s a concern? ~~Evans MJ, editor.~~ PLoS Pathog. 2023. 19(3):e1011223. doi:10.1371/journal.ppat.1011223. ~~https://dx.plos.org/10.1371/journal.ppat.1011223.~~

Wang TT, Sewatanon J, Memoli MJ, Wrammert J, Bournazos S, Bhaumik SK, Pinsky BA, Chokephaibulkit K, Onlamoon N, Pattanapanyasat K, Taubenberger JK, Ahmed R, Ravetch JV: ~~et al.~~ ~~2017.~~ IgG antibodies to dengue enhanced for FcγRIIIA binding determine disease severity. Science 2017. ~~(1979).~~ 355(6323):395–398. doi:10.1126/science.aai8128.

Wangdi K, Clements ACA, Du T, Nery SV. ~~2018.~~ Spatial and temporal patterns of dengue infections in Timor-Leste, 2005–2013. Parasit Vectors. 2018. 11(1):9. doi:10.1186/s13071-017-2588-4.

WHO. 2009. Dengue~~ENGUE~~: Guidelines ~~UIDELINES~~ for ~~FOR~~ diagnosis ~~DIAGNOSIS~~, treatment ~~TREATMENT~~, prevention ~~PREVENTION~~ and ~~AND~~ control ~~CONTROL~~. Geneva, Switzerland. Pp 1-144.

WHO. 2023. Dengue and severe dengue. [accessed 2023 May 15]. https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue.

WHO South-East Asia. 2023. Dengue in South-East Asia. WHO Regional office for South-East Asia.:1–6.

WHO-Bangladesh. 2022. Dengue - Bangladesh. https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON424.

Yuan H-Y, Liang J, Lin P-S, Sucipto K, Tsegaye MM, Wen T-H, Pfeiffer S, Pfeiffer D. ~~2020.~~ The effects of seasonal climate variability on dengue annual incidence in Hong Kong: A modelling study. Sci Rep. 2020. 10(1):4297. doi:10.1038/s41598-020-60309-7.

Yue S, Pilon P. ~~2004.~~ A comparison of the power of the t test, Mann-Kendall and bootstrap tests for trend detection / Une comparaison de la puissance des tests t de Student, de Mann-Kendall et du bootstrap pour la détection de tendance. Hydrological Sciences Journal. 2004. 49(1):21–37. doi:10.1623/hysj.49.1.21.53996. ~~https://www.tandfonline.com/doi/full/10.1623/hysj.49.1.21.53996.~~

Tables and Figure Legends:

Tables:

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

Figures:

Fig 1A: Number of dengue cases and deaths over the period 2000-2022, Bangladesh. **1B:** Number of monthly dengue cases and deaths recorded in Bangladesh, 2000-2022.

Fig 2: The boxplot compares monthly rainfall in Dhaka city, Bangladesh between two decades (2000-2010 vs 2011-2022). The bottom and top of the box indicate the first and third quantiles, the band inside the box is the median. The dots outside the box are individual outliers. Most of the months in the second decade had outlier rainfall whereas in the first decade, only the cooler months (Nov-Jan) had some extreme rainfall.

Fig 3: Top: Mean monthly growth factor for the period of 2000-2022. **Bottom:** The Monthly growth factor for the individual year 2000-2022. The horizontal dashed line indicates monthly growth factor 1 (the same number of dengue cases in two subsequent months).

Fig 4: The observed and forecasted number of dengue cases in Bangladesh using the autoregressive moving average (ARIMA) model including a 95% confidence interval.

Tables

Table 1:

	First decade (2000-2010)	Recent decade (2011-2022)	p-value
Mean annual dengue cases (interquartile range [IQR])	2216.64 (480-3182)	18321.92 (1405-28429)	0.219
Mean annual dengue deaths (IQR)	21.18 (0.0-28.5)	46.58 (3.0-105.0)	0.853
Mean Case-fatality ratio (± SD)	0.69 (±0.79)	0.23 (±13)	0.08
Mean annual temperature °C (±SD)	26.35 (±0.49)	26.84 (±0.37)	<0.001
Mean annual rainfall in mm (±SD)	2078.66 (±459.68)	1764.50 (±448.32)	0.188

Figures

Fig 1:

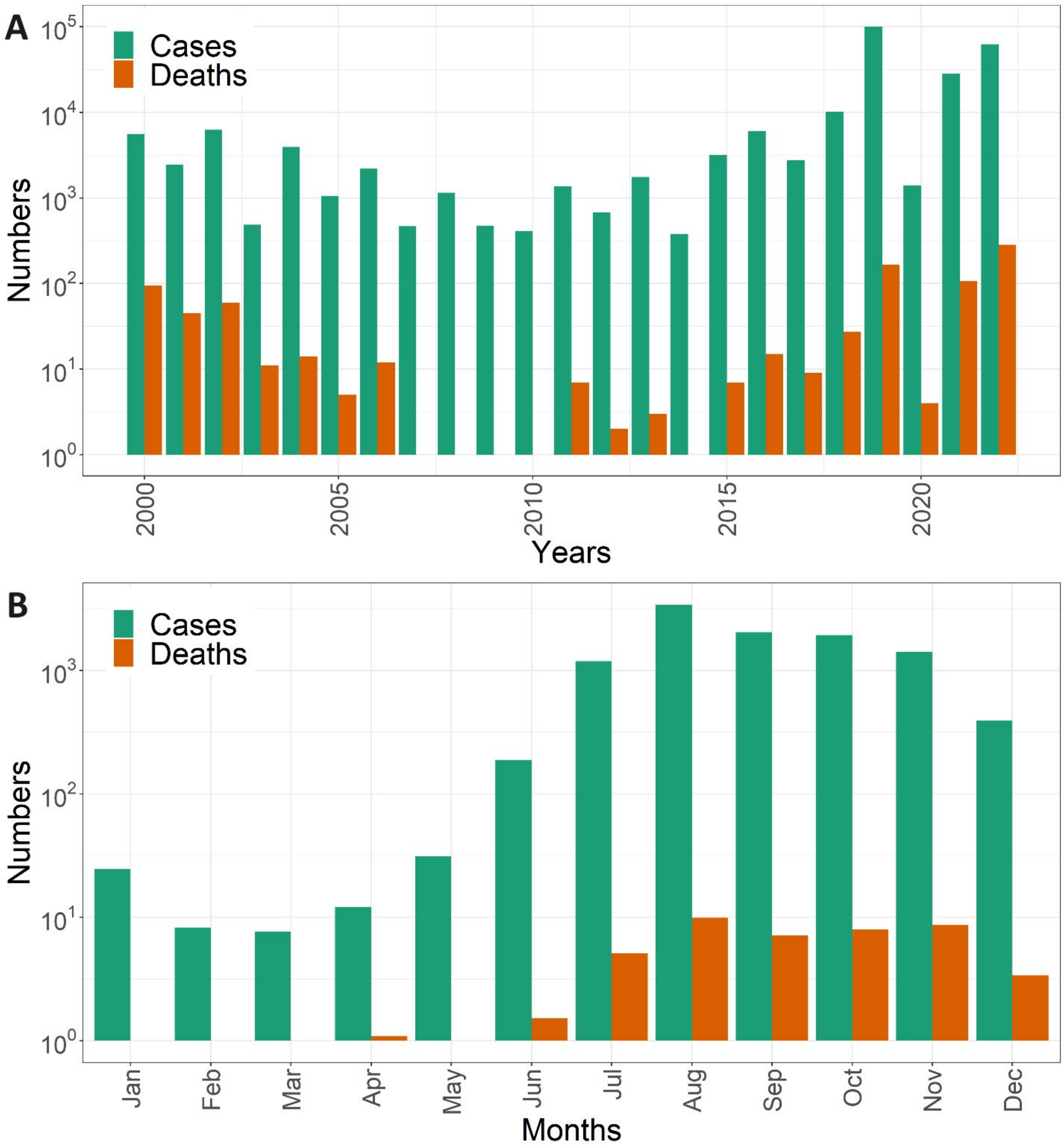


Fig 2:

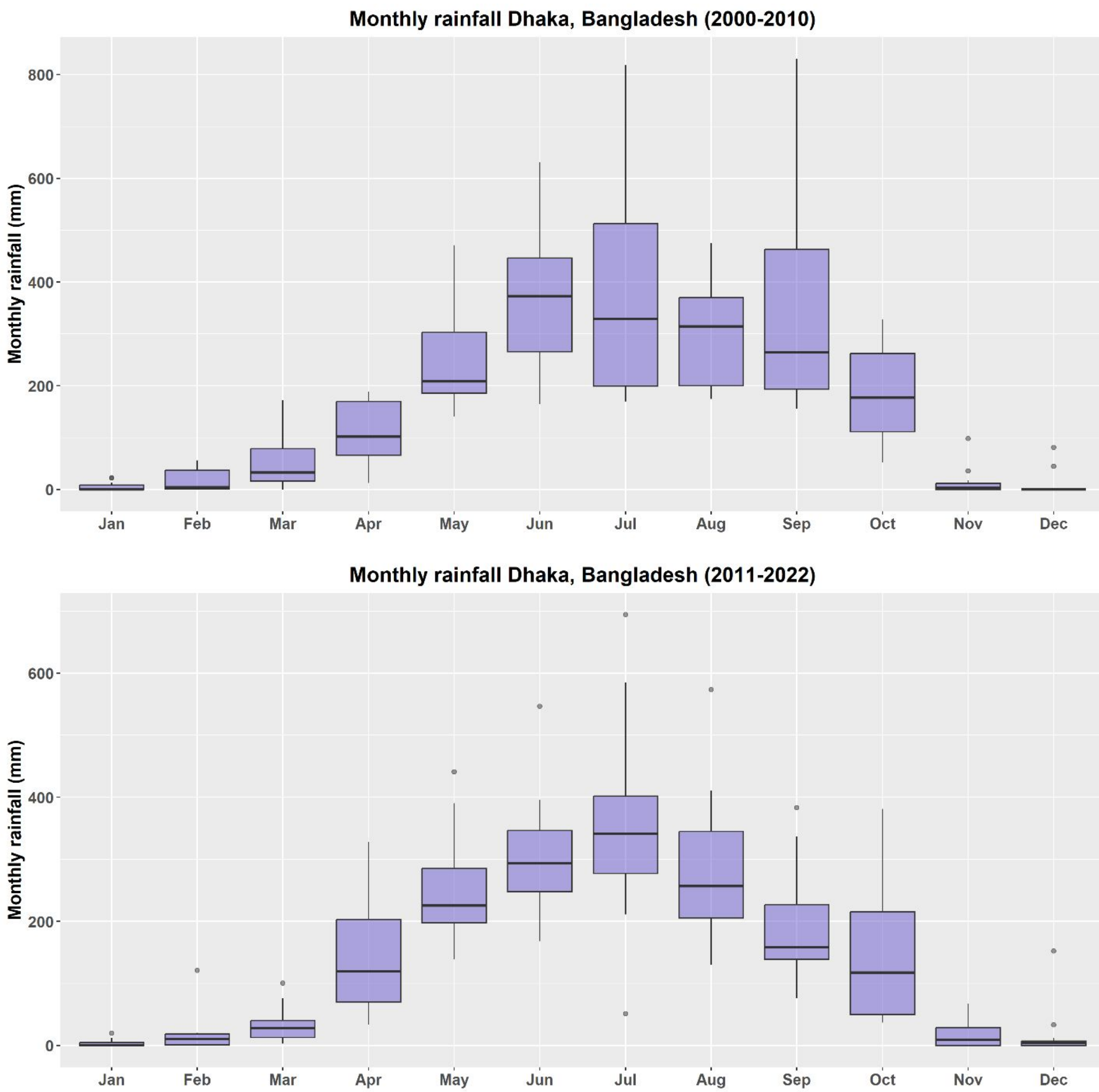

Monthly rainfall Dhaka, Bangladesh (2000-2010)
Monthly rainfall (mm)
800
600
400
200
0
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec
Monthly rainfall Dhaka, Bangladesh (2011-2022)
Monthly rainfall (mm)
600
400
200
0
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec

Fig 3:

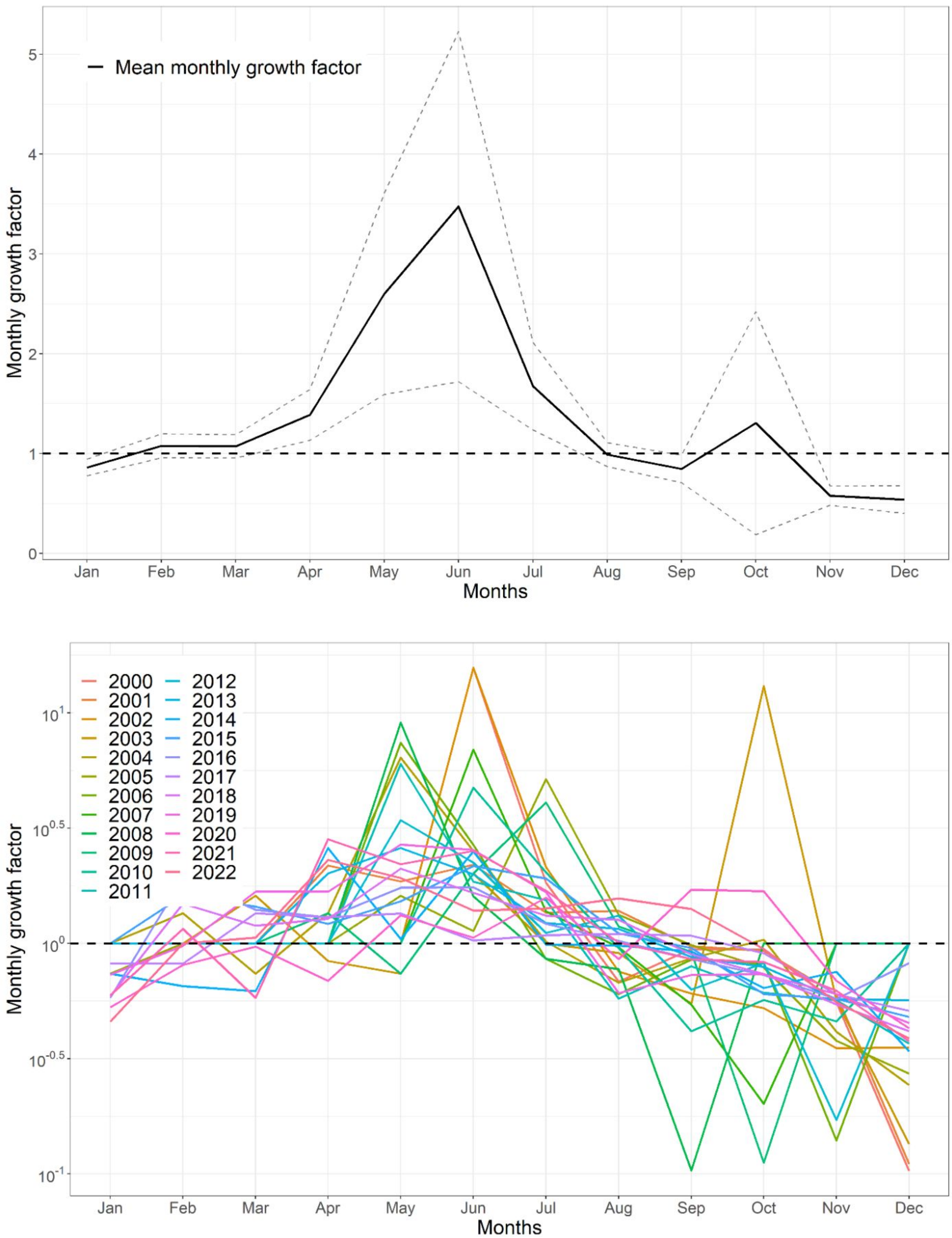
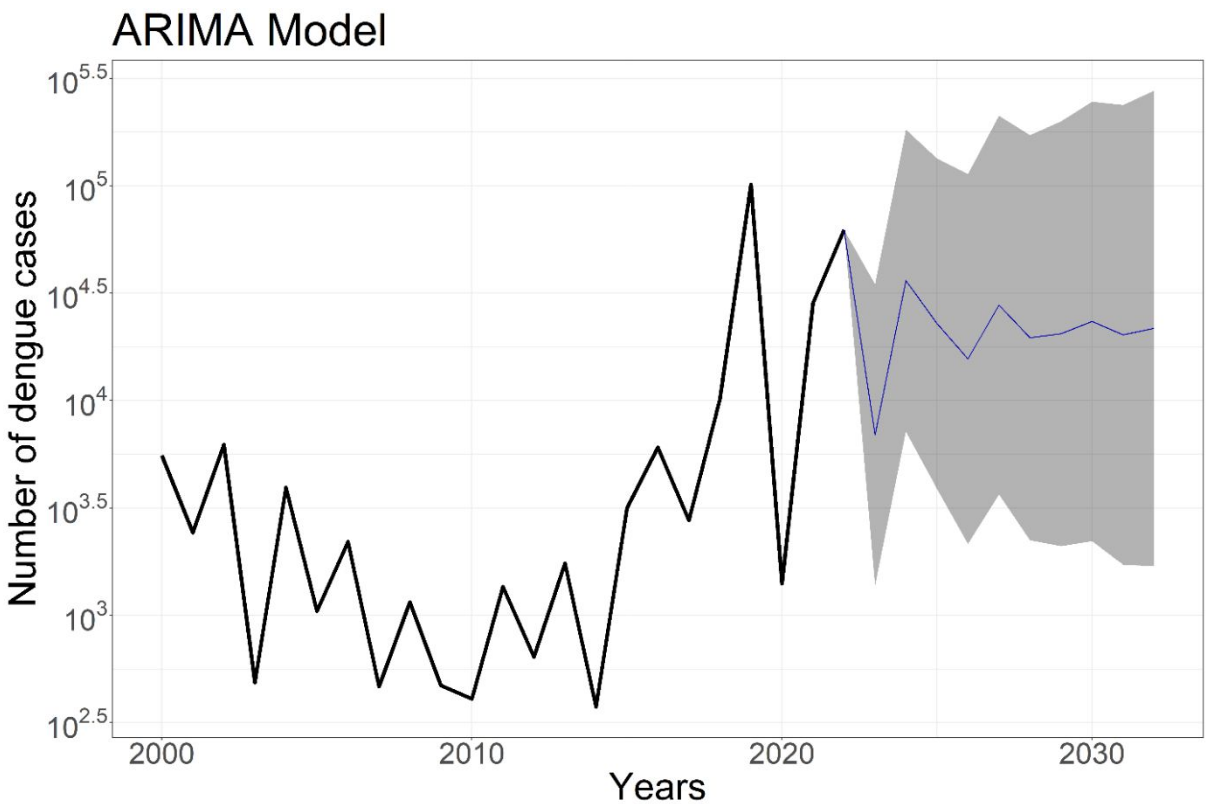

Mean monthly growth factor
Monthly growth factor
0
1
2
3
4
5
Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec
Months
2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011
2012 2013 2014 2015 2016 2017 2018 2019 2020 2021 2022
10^{-1}
$10^{-0.5}$
10^{0}
$10^{0.5}$
10^{1}

Fig 4:


ARIMA Model
Number of dengue cases
$10^{5.5}$
10^{5}
$10^{4.5}$
10^{4}
$10^{3.5}$
10^{3}
$10^{2.5}$
2000
2010
2020
2030
Years

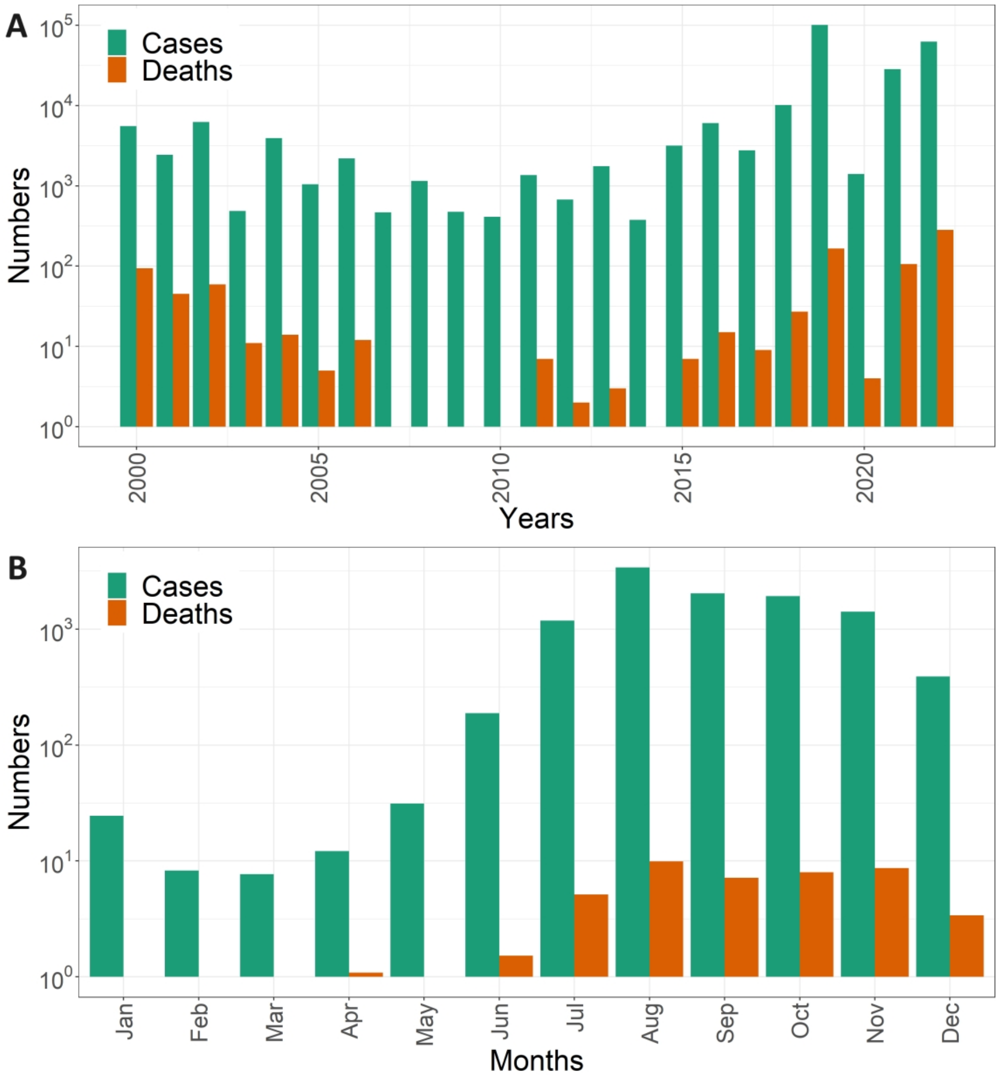


Fig 1A: Number of dengue cases and deaths over the period 2000-2022, Bangladesh. 1B: Number of monthly dengue cases and deaths recorded in Bangladesh, 2000-2022.

304x330mm (300 x 300 DPI)

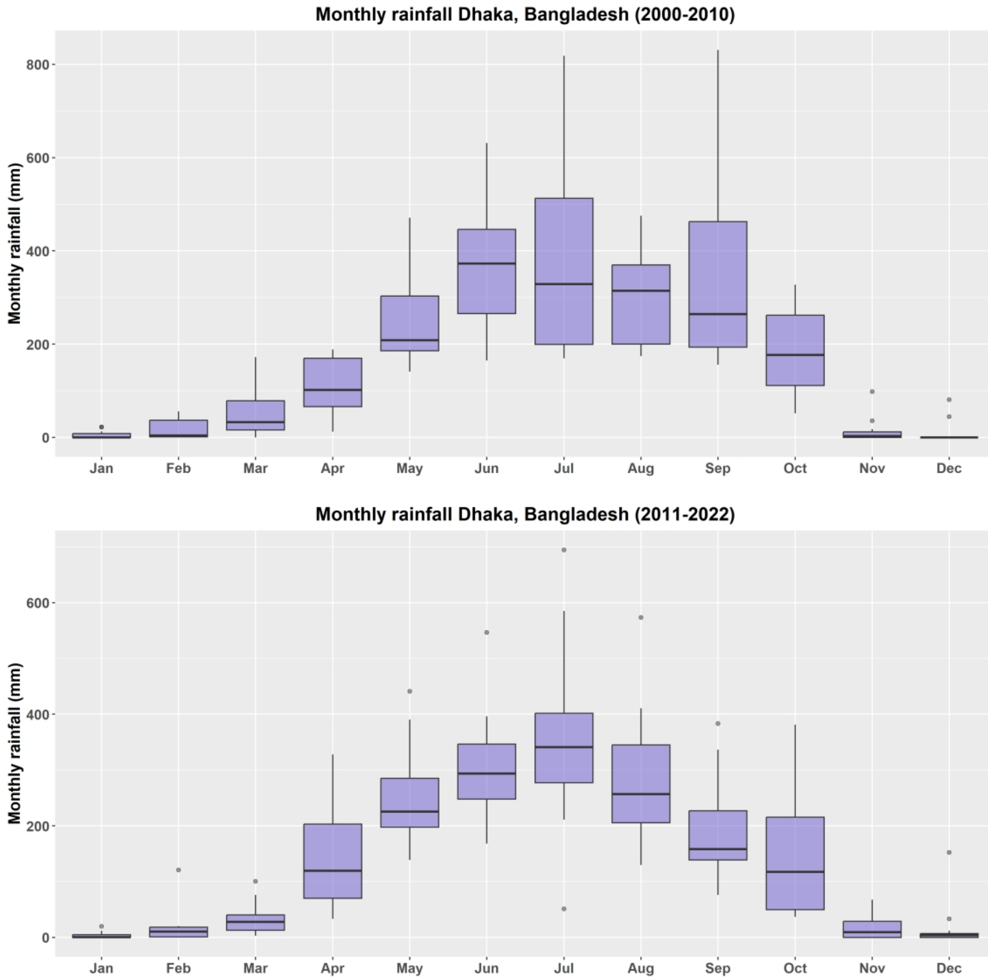


Fig 2: The boxplot compares monthly rainfall in Dhaka city, Bangladesh between two decades (2000-2010 vs 2011-2022). The bottom and top of the box indicate the first and third quantiles, the band inside the box is the median. The dots outside the box are individual outliers. Most of the months in the second decade had outlier rainfall whereas in the first decade, only the cooler months (Nov-Jan) had some extreme rainfall.

304x304mm (300 x 300 DPI)

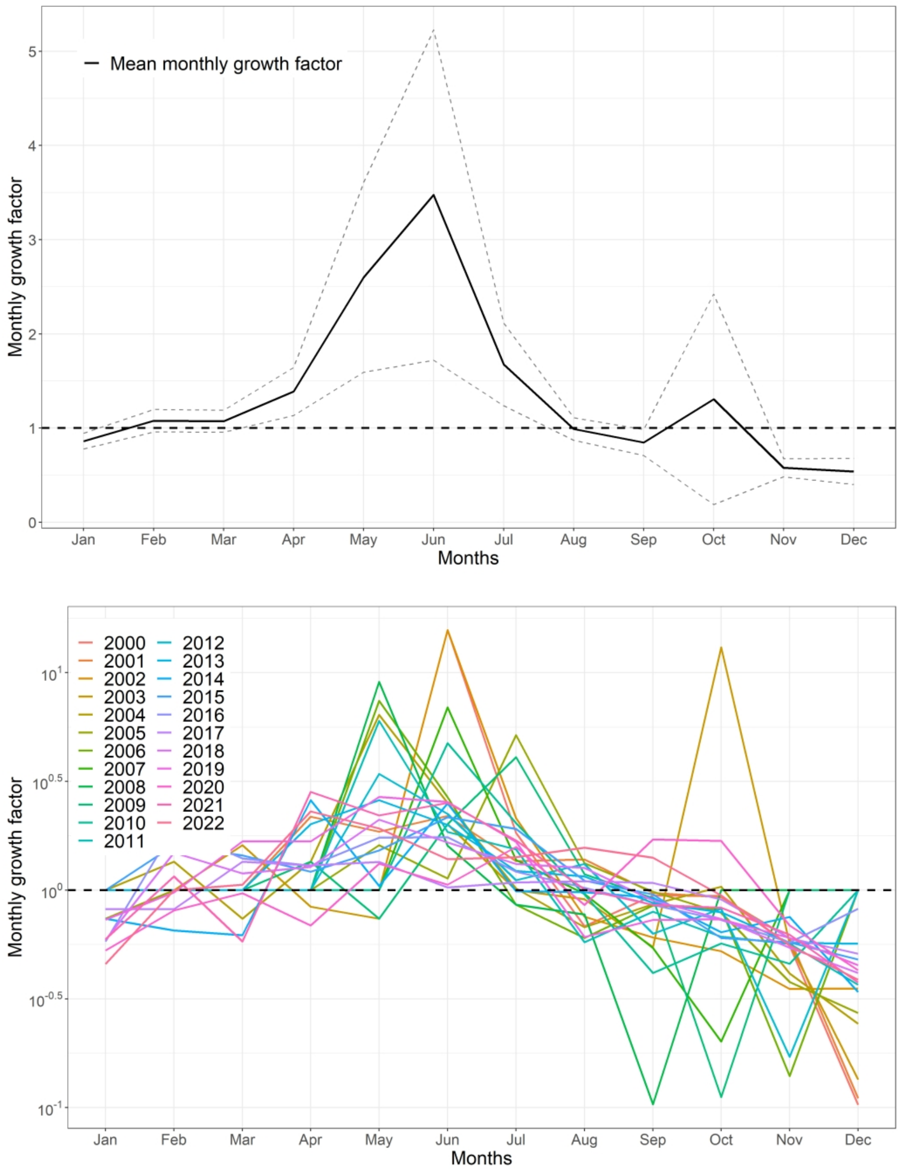


Fig 3: Top: Mean monthly growth factor for the period of 2000-2022. Bottom: The Monthly growth factor for the individual year 2000-2022. The horizontal dashed line indicates monthly growth factor 1 (the same number of dengue cases in two subsequent months).

304x406mm (300 x 300 DPI)

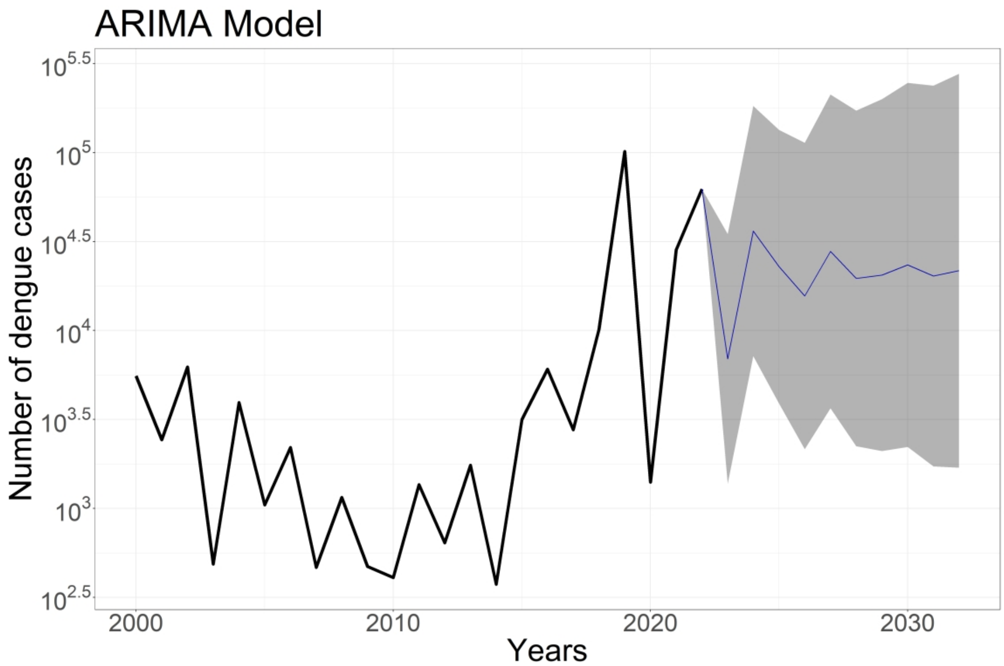


Fig 4: The observed and forecasted number of dengue cases in Bangladesh using the Autoregressive moving average (ARIMA) model including a 95% confidence interval.

457x304mm (300 x 300 DPI)