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**Title: The 2023 Deadly Dengue Outbreaks in Bangladesh Highlights a Paradigm Shift of geographical distribution of cases**

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**Abstract:**

Introduction:

Bangladesh is currently experiencing one of the largest and deadliest dengue outbreaks by reporting the highest-ever recorded annual cases and annual deaths by dengue virus (DENV) infection. Between 1 January and 30 September 2023, Bangladesh reported a total of 203,406 cases and 989 deaths with a case-fatality ratio of 0.49% 1. Historically, most of the dengue cases in the country have been reported in urban areas, with a particular concentration in the capital city of Dhaka 2 except a few year like 2019 when almost half of the cases were reported from outside Dhaka 3. Sporadic cases of dengue were documented in Dhaka in the 1960s, preceding the significant outbreak that occurred in 2000 in major cities, including Dhaka, Chittagong, and Khulna 2 4. Serological study conducted across the country demonstrated substantial spatial heterogeneity in seropositivity with seroprevalence ranging from as high as 88% in urban Chittagong to as low as 3% in rural Maulvibazar in Sylhet division 5. In the capital city Dhaka city, the seropositivity of DENV ranged from 36 to 85% 5 . Except in a few years like 2019 when Bangladesh recorded the highest number of dengue cases until that time, most cases were reported from Dhaka3,6. However, the 2023 outbreak in Bangladesh revealed a paradigm shift in the occurrences of cases in variable geographic regions. Out of 203,406 cases, 120,184 (59%) were reported from outside Dhaka, whereas only 41% of cases (n=83,222) were recorded in the capital city Dhaka. Although more than half of the cases were recorded outside Dhaka, more than 65% (639 of 989) deaths were recorded in Dhaka. We discussed the geographical shift of dengue cases as well as the possible consequences of this geographical shift, especially in rural areas. We further discussed possible explanations for a higher case-fatality ratio (CFR) of DENV infection in Bangladesh in 2023 which is 10 times higher than WHO’s goal to limit the dengue-related CFR below 0.05% 7. We used publicly available data shared by the Ministry of Health and Family Welfare to compare the DENV cases and CFR related to DENV infection between Dhaka and the rest of the country in different periods to understand the dispersion of dengue cases in the country.

**Aim:**

1. To summarize the key findings of the 2023 dengue outbreak in Bangladesh (Person, place time) Age, gender, district
2. To characterize the geographical transmission dynamics of dengue virus in Bangladesh (Relative contribution of each divisions per month)
3. To describe the Case-fatality ratio (CFR) of the dengue virus during 2023 outbreaks between Dhaka and outside

**Methods:**

Source of the data:

Definition of dengue cases:

**Relative increase of dengue cases by division**

We have estimated monthly relative changes of dengue cases in each division. The relative changes (increase of decrease) of a division (e,g. Chattogram) of dengue cases for a month (e.eg. February) were estimated with the formula as shown below -(Total number of cases reported in Chattogram division in February 2023) / Total number of cases reported in Bangladesh in February 2023) \*100

RCt is the relative changes of dengue cases in t month, CXt is the number of dengue cases in reported in X city, Nt is the total number of cases in Bangladesh in t month. To avoid any complication of 0 cases in any city in any month we added 1 dengue case in both numerator and denominator.

**Results**

1. **Results 1: Fig (Panel A - top):** Boxplot on dengue cases between 2000-2022 and a line graph of dengue cases in 2023 by Months (Jan – Dec)

**Fig (Panel B - bottom)** Boxplot on dengue cases between 2000-2022 and a line graph of dengue cases in 2023 by Months (Jan – Dec)

[Fig 1 should be Similar to Fig 2]

1. **Results 2.** Fig 2: rainfall and temperature of 2000-2022 vs 2023. Figures already created. need to be updated with Weather station data from Dhaka until 31 December
2. **Results 3:** relative change/ contribution of dengue cases in each division by months (Figure or table )
3. **Results 4:** Spreading of the dengue virus across Bangladesh. Line graph. June 28 is cut off – Eid Ul Adha
4. **Results 5:** **The distribution of dengue cases and deaths in different districts of Bangladesh, 1st Jan 2023 – 31st December 2023. Map of Bangladesh**
5. **Results 6: The correlation coefficient of dengue cases and population size (scattered plot with a fitted line). Also please check the correlation with 1) Population density 2) distance from Dhaka city**
6. **Regression model (to explain the monthly incidence of dengue in each district)**

**Monthly dengue cases of each district ~ Population size + distance from Dhaka + Presence of direct connection with Dhaka + Proxy of urbanization etc.**

**Fig 1: dengue cases and deaths** [Please Prepare this like Fig 2]



**Fig 2: Weather pattern explaining the large number of cases**

In the year 2023, an alarming surge in Dengue cases and deaths has been observed, surpassing the cumulative figures of the preceding 23 years. The cumulative data from 2000 to 2022 documented a total of 244,246 Dengue cases and 849 deaths. However, the year 2023 alone witnessed a staggering spike with 320,158 cases and 1,692 deaths, overshadowing the entire two-decade history. The comparison between the annual statistics highlights the severity of the situation. The total number of Dengue cases in 2023 is more than the combined cases from 2000 to 2022, indicating an unprecedented rise. Similarly, the death toll in 2023 alone surpasses the cumulative deaths of the past 23 years. From Figure 1, it becomes evident that each month in 2023 has reported higher cases and deaths than the corresponding months from 2000 to 2022. This monthly breakdown emphasizes the sustained intensity of the Dengue outbreak throughout the entire year.

**Fig 2 Top: Boxplot of monthly rainfall of Dhaka city for the period of 2000-2023 and line graph of monthly rainfall of Dhaka city in 2023. Bottom: Boxplot of monthly mean temperature in °C of Dhaka city for the period of 2000-2022 and a line graph of monthly rainfall of Dhaka city in 2023.**



**Fig 3 or Table 1: Monthly Relative change of dengue cases (Table or graph)**

The average rainfall from 2000 to 2022 stood at 159.56. However, in 2023, the annual rainfall increased to an astonishing 192.01, exceeding the previous long-term average. Contrary to the rising rainfall trend, the average temperature experienced a slight decline. From 26.59 in the years 2000 to 2022, the temperature decreased marginally to 26.23 in 2023. Figure 3 provides a comprehensive view of the climatic conditions throughout 2023, revealing distinctive patterns. Notably, heavy rainfall and high temperatures were observed from the outset of the year, surpassing previous records. The sustained prevalence of these conditions throughout the year, especially the extended period of rainfall, has created conducive environments for the proliferation of mosquitoes.

Table:

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Divisions | No cases in Jan | Relative increase in Feb (%) | Relative increase in Mar (%) | Relative increase in Apr (%) | Relative increase in May (%) | Relative increase in June (%) | Relative increase in July (%) | Relative increase in Aug (%) | Relative increase in Sep (%) | Relative increase in Oct (%) | Relative increase in Nov (%) | Relative increase in Dec (%) |
| Dhaka city | 272 | 46.11% | 66.96% | 64.58% | 83.41% | 78.93% | 52.72% | 40.04% | 31.66% | 23.53% | 21.29% | 23.08% |
| Dhaka division (Except Dhaka city) | 58 | 10.18% | 2.68% | 2.08% | 3.09% | 3.36% | 11.10% | 16.39% | 19.26% | 23.05% | 22.99% | 22.17% |
| Mymensingn | 7 | 1.80% | 1.79% | 1.39% | 1.25% | 1.61% | 2.68% | 3.16% | 2.65% | 2.02% | 2.29% | 2.96% |
| Chittagong | 140 | 23.95% | 16.07% | 23.61% | 7.91% | 8.11% | 13.36% | 14.98% | 15.13% | 13.22% | 11.24% | 14.72% |
| Khulna | 24 | 4.19% | 4.46% | 3.47% | 0.77% | 1.98% | 3.97% | 6.27% | 10.32% | 15.64% | 19.49% | 17.79% |
| Rajshahi | 7 | 0.60% | 0.89% | 0.69% | 0.10% | 0.45% | 2.33% | 4.32% | 5.52% | 8.60% | 10.49% | 8.42% |
| Rangpur | 2 | 0.60% | 0.89% | 0.69% | 0.10% | 0.47% | 1.85% | 2.40% | 1.68% | 1.53% | 1.13% | 1.64% |
| Barishal | 53 | 16.77% | 12.50% | 8.33% | 3.95% | 4.58% | 11.12% | 11.75% | 13.46% | 12.18% | 10.95% | 9.16% |
| Sylhet | 3 | 0.60% | 0.89% | 0.69% | 0.19% | 0.64% | 0.88% | 0.71% | 0.32% | 0.24% | 0.16% | 0.16% |

In the initial month of 2023, Dhaka City, Dhaka Division (excluding Dhaka City), Mymensingh, Chittagong, Khulna, Rajshahi, Rangpur, Barisal, and Sylhet reported 272, 58, 7, 140, 24, 7, 2, 53, and 3 Dengue cases, respectively. The highest relative increase occurred in Dhaka City during May (83.41%), contrasting with the minimal increases in Khulna and Rajshahi during the same period (0.10%). However, as relative changes diminished in Dhaka City, other districts experienced a rise, closely resembling the patterns observed in Dhaka City and Dhaka Division (excluding Dhaka City) by October, constituting a 23% increase. A notable transformation emerged after October, where a substantial decline in the overall relative increase transpired across divisions in 2023. This reduction persisted in the subsequent months.

A graph of different colored lines and numbers

Description automatically generated

**Figure 4: The spreading of dengue cases between Dhaka and outside Dhaka before and after Eid ul Adha**



**Legnd Figure 4-- [The line graph of dengue virus infection in the capital city Dhaka and outside from 1 January to 25 August 2023. A large proportion of people living in the capital city left Dhaka when Eid-Al-Adha was celebrated on 28th June.]**

The pattern of Dengue cases exhibited a parallel trajectory in both Dhaka City and areas beyond Dhaka City in mid-April. However, after this period, Dhaka City exclusively displayed an elevated trend until the beginning of August. Following this, Dengue cases in areas outside Dhaka City surpassed. Notably, Dengue-related deaths were initially higher outside Dhaka City until February, after which an escalation within Dhaka City commenced and persisted.

**Fig 5: The distribution of dengue cases and deaths in different districts of Bangladesh, 1st Jan 2023 – 8th Sep 2023.**



Dhaka reported the highest incidence of dengue with 112,958 cases, followed by Chittagong (14,150), Barisal (13,560), Manikganj (12,932), and Patuakhali (7,576). Conversely, the lowest Dengue cases were recorded in Sunamganj (102), Maulvibazar (129), Panchagarh (187), Joypurhat (263), and Lalmonirhat (305). In terms of Dengue-related deaths, Dhaka reported the highest death toll at 976, trailed by Barisal (163), Faridpur (137), Chittagong (105), and Khulna (40).

**Fig 6: The correlation coefficient of DENV-infected cases admitted in hospitals in different districts and it’s population size. A positive correlation exists with the number of inhabitants of the cities.**



In the analysis of district-level data, a positive correlation was observed between population size and both the incidence of Dengue cases and deaths. As the population size increases, there is a concurrent increase in Dengue outcomes. A similar association is evident in the relationship between population density and Dengue outcomes, where districts with higher population density also exhibit higher Dengue cases and deaths. Conversely, a negative correlation was identified between the distance of each district from Dhaka city and the occurrence of Dengue cases. An increase in distance from Dhaka city corresponds to a decrease in Dengue cases in the respective district.

Results 7: regression model

Monthly dengue case of each district ~ Population size + distance from Dhaka + Presence of direct connection with Dhaka + Proxy of urbanization etc.

Table 2. The negative binomial regression models for outcome (Dengue cases) and other explanatory variables

|  |  |  |
| --- | --- | --- |
| Outcome variables | IRR (95% CI) | P-value |
| Deaths | 1.01 (1.01-1.02) | 0.002 \*\* |
| Sex (male to female) ratio | 0.99 (0.97-1.01) | 0.073 |
| Urban-rural ratio | 1.01 (0.99-1.01) | 0.536 |
| Population density | 0.99 (0.99-1.00) | 0.341 |
| Distance from Dhaka (capital city) | 0.99 (0.98-0.99) | 0.009 \*\* |
| **Connection with Dhaka (by Vehicle)** |  |  |
| Yes | 0.90 (0.32-1.98) | 0.806 |
| No | Reference | - |

Statistical analysis:

We expanded our dataset by incorporating district-wise information as outcome variables, sourced from the BBS 2022 report. These variables included the Sex ratio (calculated as the male population divided by the female population in each district), urban-rural ratio (calculated by dividing the urban population by the rural population), population size, and area of each district. Additionally, we calculated population density by dividing the population size by the area of each district. Moreover, we considered the distance of each district from Dhaka, by road connection. Subsequently, we conducted a negative binomial regression analysis the association of these outcome variables on Dengue cases using the 2023 data. We select a negative binomial model, as opposed to a Poisson regression model, was informed by the observation that the variances exceeded the means in the outcome variables. The results of our model are presented as incidence rate ratios (IRRs), adjusted for dengue deaths, sex ratio, urban-rural ratio, population density, distance from Dhaka, and connection with Dhaka, with associated 95% confidence intervals.

Results:

In the negative binomial regression model, a statistically significant positive association was identified between the number of dengue deaths in a district (Incidence Rate Ratio [IRR]: 1.01, 95% Confidence Interval [CI]: 1.01-1.02) and the occurrence of dengue cases. Conversely, a significant negative association was observed between the distance of each district from Dhaka city and the incidence of dengue cases (IRR: 0.99, 95% CI: 0.98-0.99). While the sex ratio and population density exhibited slight negative associations, and the urban-rural ratio showed a slight positive association with dengue cases, these relationships did not show statistical significance according to the negative binomial regression model.

**Discussion:**

**The higher CFR of DENV in Bangladesh**

The CFR of primary DENV infection is generally low with an estimated value of 0.01-0.1%, but the CFR could reach up to 1-4% for secondary or tertiary DENV infection. In the past 23 years, Bangladesh recorded a CFR of 0.34% which is high compared to other countries in the region 6. In 2023, the CFR is much higher (0.50%) which is inflated by a very high fatality rate in the capital city Dhaka (0.6%). The high CFR in Dhaka city can be explained as a possible higher rate of secondary or tertiary cases as more than 80% of people in Dhaka city were exposed to any one serotype of DENV in the past 5. Moderate to severe cases outside of Dhaka city are referred/travelled to hospitals in Dhaka for better health care, especially for ICU needs. WHO’s situation report reveals that 41% of the death cases were referred to larger cities, especially Dhaka 17. More than 44% of patients with DENV infection admitted to hospitals in Dhaka city were from outside Dhaka 11. Also, there is a more regular and organized notification of deaths from Dhaka city as compared to other parts of the country where some of the deaths are unreported. Bangladesh surveillance is only based on selected hospital admissions which account for approximately 5% of total hospitals in the county, and the patients outside these hospitals as well as private clinics and those not attending any health care settings are not included 11 Thus, current surveillance misses a large number of patients in the denominator of the CFR estimation. However, moderate and severe patients are likely to be admitted in hospitals and thus the deaths are missed less compared to the infected cases. Thus, it might be worth mentioning that the CFR that we are reporting is more of a CFR for moderate and severe dengue cases, as the denominator might miss a substantial proportion of non-severe dengue cases.

**The largest outbreak in Bangladesh:**

A number of drivers contributed in the largest outbreak of dengue fever in Bangladesh. First, the dengue serotype -2 (DENV-2) has reappeared in Bangladesh after 2018 8. The absence of the serotype allowed a large proportion of the population to be naïve as the city experienced more than 4% annual growth of population. Second, the outbreak in 2022 continued to 2023 with a relatively warm year and late rain the season allowing more than 5024 cases in December 2022 compared to the monthly mean of 188 cases for December in Bangladesh (2000-2021) 8. Thus, the year 2023 started with a large number of cases including 566 cases in January compared monthly mean of 126 cases in Bangladesh (2000-2021) 8. Third, unusually high rainfall in the pre-monsoon season allowed the breeding of mosquitoes with higher numbers leading to a large outbreak in the county.

**Spread of DENV throughout Bangladesh**

Dhaka is one of the most densely populated cities in the world with more than 22 million people living in approximately 300 squares kilometres with a population density of 23,234 people/KM2 9. Many people travel to their rural home during two large festivals: Eid-Al-Fitr and Eid-Al-Adha. In 2023, the Eid-Al-Adha was celebrated on 28th June. Up until 28th June 2023, a total of 7862 patients were recorded in the country of which 6014 (76.5%) were recorded in the capital city. Approximately 60% of people infected with DENV do not show any clinical symptoms 10. In Bangladesh, only a small fraction of people infected with DENV are captured in the current surveillance system as the data is gathered from approximately 5% of the total hospitals or diagnostic centres of the country11. More than 15 million people left Dhaka and its surrounding cities to celebrate Eid-Al-Adha with their families in rural Bangladesh12. This large movement probably played a role in spreading the DENV virus throughout the county. People infected with DENV can remain viremic (infectious) for a maximum of 12 days 13. Although *Aedes* *aegypti*, the key vector of DENV transmission is a city-adapted mosquito, the Asian tiger mosquito, *Aedes albopictus,* the secondary vector of DENV is adapted more to rural settings. Earlier studies in Bangladesh reported the presence of *Ae albopictus* in different parts of Bangladesh 5,14. As competent vectors (*Ae albopictus*) were documented outside Dhaka, it is possible to maintain local transmission if dengue is introduced to the rural areas in Bangladesh. In 2023, it seems like that infected people travelled from Dhaka to rural areas and spread the virus to the rural areas where *Ae albopictus* mosquito maintained the local transmission 11. The earlier start of the monsoon this year (ref) also coincided with this and further influenced the growth of the vector population in the rural areas15. By 25 July 2023, all 64 districts reported at least one DENV infection in their hospitals. In that specific time, a total of 37, 688 patients were recorded in the country of which 22349 (59.30%) were recorded in the capital city. The spreading of DENV across the country might have severe consequences for the ongoing outbreak and the coming years. The rural cycle of DENV transmission is usually led by *Ae albopictus* and there is some specific difference that makes *Ae albopictus* a crucial vector for DENV **(Table 2)**.

Until the reappearance of DENV-serotype 3 in 2019, the DENV virus was mostly endemic in urban settings with a large portion of people being exposed to the virus in their lifetime 5. The distribution of *Ae. aegypti* which is an urban-dwelling mosquito probably played a role in such high seroprevalence 5. This high seroprevalence in the large cities, especially in metropolitan Dhaka created the opportunity of exposing to second, third, or fourth infection with heterogenous serotypes. The top five districts with higher CFR for DENV infection are Faridpur (1.45%), Satkhira (0.80%), Barisal (0.78%), Dhaka (0.75%), and Chittagong (0.75%). All four serotypes of the dengue virus have been recorded in Bangladesh at different times since 2000. DENV- Serotype 3 caused a larger outbreak in 2019 and remained a dominant serotype until 2022. DENV-4 reappeared in the year 2022 with co-circulation of DENV-1 and DENV-3. In 2023, DENV-2 became a predominant serotype (62%) along with DENV-3 (29%) and co-infection of DENV-2 and DENV-2 (10%) 16. Thus, exposure to heterogenous serotypes increases the risk of severe dengue infection due to secondary and/or tertiary dengue infection which has a much higher CFR than the primary infection 13. The number of reported cases in a different district in Bangladesh is correlated with the population size (r=0.76, p<0.001) of the district **(Fig 2).**

Conclusion:

**Table 1:** Monthly relative changes in dengue cases in each division in Bangladesh

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Divisions | Jan  Case  (change %) | Feb  Case  (Change %) | Mar  Case  (Change %) | Apr  Case  (Change %) | May  Case  (Change %) | June  Case  (Change %) | Jul  Case  (Change %) | Aug  Case  (Change %) | Sep  Case  (Change %) | Oct  Case  (Change %) | Nov  Case  (Change %) | Dec  Case  (Change %) |
| Dhaka city | 272 (48%) | 348- 272 = 76 (45.78%)  46.11% | 66.96% | 64.58% | 83.41% | 78.93% | 52.72% | 40.04% | 31.66% | 23.18% |  |  |
| Dhaka division (Except Dhaka city) | 58 (10) | 78 - 58= 20  12.04%  10.18% | 2.68% | 2.08% | 3.09% | 3.36% | 11.10% | 16.39% | 19.26% | 22.37% |  |  |
| Mymensingh | 7 (1.2%) | 1.80% | 1.79% | 1.39% | 1.25% | 1.61% | 2.68% | 3.16% | 2.65% | 2.11% |  |  |
| Chittagong | 140 (25%) | 23.95% | 16.07% | 23.61% | 7.91% | 8.11% | 13.36% | 14.98% | 15.13% | 14.35% |  |  |
| Khulna | 24 (4%) | 4.19% | 4.46% | 3.47% | 0.77% | 1.98% | 3.97% | 6.27% | 10.32% | 14.62% |  |  |
| Rajshahi | 7 (1.2%) | 0.60% | 0.89% | 0.69% | 0.10% | 0.45% | 2.33% | 4.32% | 5.52% | 7.99% |  |  |
| Rangpur | 2 (0.4%) | 0.60% | 0.89% | 0.69% | 0.10% | 0.47% | 1.85% | 2.40% | 1.68% | 2.02% |  |  |
| Barisal | 53 (9%) | 16.77% | 12.50% | 8.33% | 3.95% | 4.58% | 11.12% | 11.75% | 13.46% | 13.06% |  |  |
| Sylhet | 3 (0.3%) | 0.60% | 0.89% | 0.69% | 0.19% | 0.64% | 0.88% | 0.71% | 0.32% | 0.40% |  |  |
| Total | 566 (100%) | 166 (100%) | 100% |  |  |  |  |  |  |  |  |  |

**Conclusion:**

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