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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 experienced it’s largest and deadliest dengue outbreak by reporting the highest-ever recorded annual cases and deaths by dengue virus (DENV) infection in 2023. Between 2000-2022, Bangladesh reported a total of 244,246 dengue cases including 849 deaths with a case-fatality ratio of 0.49% 1. In 2023 alone, the number of cases and deaths surpasses the previous 23 years' cumulative numbers: 320,835 cases and 1,699 deaths until 27 December 2. While this number is shocking and concerning, epidemiologically these figures are not unexpected based on the trend of dengue cases in the last five years: during this period (2018-2022), more than 82% of cases (n=202,425) and 69% of deaths (n=550) of last 23 years were reported 1. There was an increasing trend of dengue cases and resulting deaths in Bangladesh 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 3 except a few years like 2019 when almost half of the cases were reported from outside Dhaka 4. 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 3 5. Serological studies 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 6. In Dhaka city's capital, the seropositivity of DENV ranged from 36 to 85% 6. However, the 2023 outbreak in Bangladesh revealed a paradigm shift in the occurrences of cases in variable geographic regions. Of 320,835 cases, 207,716 (65%) were reported from outside Dhaka. Although more than half of the cases were recorded outside Dhaka, more than 58% (979 of 1699) deaths were recorded in Dhaka.

The objective of this study was to summarize the key findings of the 2023 dengue outbreak in Bangladesh, to characterize the geographical transmission dynamics of dengue virus in Bangladesh (Relative contribution of each division per month), and to characterize the spreading dengue virus between Dhaka and outside the capital city.

**Methods:**

**Source of the data:** We collected the data on dengue cases and deaths record from daily press release of Management Information System (MIS) of the Ministry of Health and Family Welfare, Bangladesh. The MIS defined 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 7. MIS collected dengue case data from 77 hospitals based on in Dhaka city (20 public and 57 private hospitals) and the central district hospital of 63 other districts of the country including the hospitalized patients in tertiary care medical college hospitals (Ref: JME paper 2023).

We collected meteorological data (3-hourly temperature and daily rainfall) from the Bangladesh Meteorological Department (BMD) over the period 2000–2023 from the meteorological station located in Mirpur, Dhaka (Lat 23.78, Lon 90.38).

**Relative increase of dengue cases by division**

We have estimated monthly relative changes in dengue cases in each division. The relative changes (an increase or decrease) of a division (e,g. Chattogram) of dengue cases for a month (e.g. 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.

**Statistical Analysis**

We expanded our dataset by incorporating district-wise dengue case data as outcome variables. We further collected district-wise data from the Statistical Yearbook Bangladesh 2022 published by the Bangladesh Bureau of Statistics (Ref) including population size, the ratio of rural and urban population, and distance from the capital city, Dhaka. Additionally, we calculated population density by dividing the population size by the area of each district. Subsequently, we ran a negative binomial regression analysis of the association of the total number of dengue cases in 2023.

We selected a negative binomial model, as opposed to a Poisson regression model, as the observation that the variances exceeded the means in the outcome variables (likelihood ratio test, p-value<0.05). 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:**

During 2023 (1 Jan to 31 December), a total of 320,835 dengue cases have been reported with 1,699 deaths (case fatality ratio: 0.53%) **(Fig 1)**. The number of cases reported in 2023 is 1.3 times higher than the number of reported cases in the past 23 years (565,081 vs 244,246) and two times more deaths than the number of fatalities recorded in the past 23 years (1699 vs. 849) in the country **(Fig 1)**.

The number of reported cases and deaths was higher in each month in 2023 compared to the average number of cases or deaths in the corresponding months from 2000 to 2022 **(Fig 1)**.



**Fig 1:** The number of dengue cases and deaths reported in 2023 vs 2000-2022 in Bangladesh. Log 10 base is used for the displaying the cases and deaths for the convenience of visualization and comparison.

Bangladesh experienced a higher amount of rainfall in 2023 compared to the average annual precipitation of the period 2000-2022. The average rainfall for the period 2000 to 2022 was 159.56 mm whereas in 2023 total annual rainfall increased to 197.84 mm **(Fig 2)**. It was also evident that rainfall started earlier in the year with 130.5 mm of precipitation in March compared to an average of 45.0 mm amount of rainfall for the month of the period 2000-2022. There was a comparable range of temperature between 2023 and the period 2000-2022. In comparison to the mean temperature of 26.59 °C for the period 2000 to 2022, the temperature decreased marginally to 26.37 °C in 2023 **(Fig 2)**.



**Fig 2:** The temperatures (°C) and precipitation (mm) of Bangladesh as recorded in a Weather station in Mirpur Dhaka, by Bangladesh Meteorological Department, Bangladesh for the period 2000-2022 vs. 2023.

**Relative changes of dengue cases in each division:**

Dhaka city has been the main outbreak side in 2023 and contributed in more than 50% of the total cases up until July and then cases started to increase outside the country. Outside Dhaka city, Dhaka division (excluding Dhaka city) and Chittagong division have been among the prominent sites of the outbreak **(Fig 3/ Table 1)**. In May, Dhaka city contributed more than 83% of the total cases in the country. The Sylhet division contributed less than 1% of cases throughout the year. The relative changes in dengue cases in different divisions became more evident after July when most divisions started to report an increased percentage of cases and Dhaka city started to report a lower percentage of cases **(Fig 3).** In November, the Dhaka division (except Dhaka city) reported almost 23% of dengue cases which was the highest percentage of dengue cases for any division in the country, the first record of surpassing the number of cases reported in Dhaka city by any division of the country (**Fig 3)**.

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**Fig 3:** The relative changes of Dengue cases in each division in Bangladesh, 2023. Although Dhaka city remains the centre of the outbreak, the percentage of cases has increased outside Dhaka city after July 2023.

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 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% | 23.07% |
| 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% | 22.98% |
| Mymensingh | 7 | 1.80% | 1.79% | 1.39% | 1.25% | 1.61% | 2.68% | 3.16% | 2.65% | 2.02% | 2.29% | 3.13% |
| Chittagong | 140 | 23.95% | 16.07% | 23.61% | 7.91% | 8.11% | 13.36% | 14.98% | 15.13% | 13.22% | 11.24% | 15.26% |
| Khulna | 24 | 4.19% | 4.46% | 3.47% | 0.77% | 1.98% | 3.97% | 6.27% | 10.32% | 15.64% | 19.49% | 17.16% |
| Rajshahi | 7 | 0.60% | 0.89% | 0.69% | 0.10% | 0.45% | 2.33% | 4.32% | 5.52% | 8.60% | 10.49% | 8.23% |
| Rangpur | 2 | 0.60% | 0.89% | 0.69% | 0.10% | 0.47% | 1.85% | 2.40% | 1.68% | 1.53% | 1.13% | 1.61% |
| Barisal | 53 | 16.77% | 12.50% | 8.33% | 3.95% | 4.58% | 11.12% | 11.75% | 13.46% | 12.18% | 10.95% | 9.46% |
| Sylhet | 3 | 0.60% | 0.89% | 0.69% | 0.19% | 0.64% | 0.88% | 0.71% | 0.32% | 0.24% | 0.16% | 0.19% |

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.

When compared to the number of dengue cases in the capital city Dhaka vs. the rest of the country, there was a parallel trajectory in both Dhaka city and outside until mid-April. After that, dengue cases started to increase exponentially in the capital city Dhaka which continued up until the end of July 2023, and then the number of cases outside Dhaka surpassed the capital city. Notably, Dengue-related deaths were initially higher outside Dhaka City until February, after which an escalation within Dhaka City commenced and persisted till the end of the year.



**Fig 4: The line graph of dengue virus infection in the capital city Dhaka and outside from 1 January to 31 December 2023. A large proportion of people living in the capital city left Dhaka when Eid-Al-Adha was celebrated on the 28th of June and subsequently, dengue cases started to increase outside Dhaka.**

District-wise, Dhaka district reported the highest incidence of dengue with 113,119 cases, followed by Chittagong (14,187), Barisal (13,588), Manikganj (12,945), and Patuakhali (7,579). Conversely, the lowest Dengue cases were recorded in Sunamganj (102), Maulvibazar (129), Panchagarh (187), Joypurhat (264), and Lalmonirhat (305). In terms of Dengue-related deaths, Dhaka reported the highest death toll at 979, trailed by Barisal (164), Faridpur (138), Chittagong (106), and Khulna (41).



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

When compared with district level dengue monthly cases, a positive correlation was observed between population size and the incidence of Dengue cases (r=0.44, p=<0.001) and deaths (r=0.44, p=<0.001). As the population size increases, there is a concurrent increase in Dengue. A similar association is evident in the relationship between population density and dengue cases, where districts with higher population density also exhibit higher dengue cases (r=0.47, p=<0.001) and deaths (r=0.43, p=<0.001). Conversely, a negative correlation was identified between the distance of each district from Dhaka city and the occurrence of Dengue cases (r=-0.30, p=0.017).



**Fig 6: The correlation coefficient of dengue cases and deaths in different districts and it’s population size, population density, and distance from Dhaka city. A positive correlation exists with the population density of the district and a negative correlation exists with the distance from the capital city Dhaka.**

In the negative binomial regression model, a statistically significant negative association was identified between the distance of each district from Dhaka city and the incidence of dengue cases (Incidence Rate Ratio [IRR]: 0.995, 95% CI: 0.992-0.997) indicating that districts far away from Dhaka city had lower number of dengue cases. While population density exhibited slight negative associations, and the ratio of the urban-rural population ratio showed a slight positive association with dengue cases without statistical significance (Table 2).

|  |  |  |
| --- | --- | --- |
| Outcome variables | IRR (95% CI) | P-value |
| Deaths | 1.004 (1.001-1.007) | <0.001 |
| Urban-rural ratio | 1.006 (0.999-1.015) | 0.086 |
| Population density | 0.999 (0.998-0.999) | 0.012 |
| Distance from Dhaka (capital city) | 0.995 (0.992-0.997) | <0.001 |

**Discussion:**

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% 8. 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.

**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 1. 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 6. 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 9. More than 44% of patients with DENV infection admitted to hospitals in Dhaka city were from outside Dhaka 10. 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 10 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 11. 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) 11. 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) 11. 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 square kilometres with a population density of 23,234 people/KM2 12. Many people travel to their rural homes 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 13. 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 country10. More than 15 million people left Dhaka and its surrounding cities to celebrate Eid-Al-Adha with their families in rural Bangladesh14. 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 15. 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 6,16. 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 10. 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 areas17. 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 6. The distribution of *Ae. aegypti* which is an urban-dwelling mosquito probably played a role in such high seroprevalence 6. 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%) 18. 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 15. 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:**

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