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

**Authors:**

Mohammad Nayeem Hassan1, Mahbubur Rahman2, Meraj Uddin3, Kazi Mizanur Rahman4, Kishor Kumar Paul5, Mohammad Ferdous Rahman Sarker2, Farhana Haque6, Avinash Sharma6, Md Asaduzzaman7, Alimuddin Zumla8, **Najmul Haider9\***

**Institutional affiliations**:

1Department of Statistics, Shahjalal University of Science and Technology, Sylhet 3114, Bangladesh (MNH: [nayeem5847@gmail.com](mailto:nayeem5847@gmail.com))

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

3Birmingham City University, Birmingham, United Kingdom ([meraj.cm48@gmail.com](mailto:meraj.cm48@gmail.com) )

4Faculty of Health Sciences and Medicine, Bond University, Robina QLD 4226, Australia (KMR: [krahman@bond.edu.au](mailto:krahman@bond.edu.au))

5 The Kirby Institute, University of New South Wales, Australia

6 Department of Infectious Disease Epidemiology and Dynamics, London School of Tropical Medicine and Hygiene, London, United Kingdom, WC1E 7HT (Farhana.Haque@lshtm.ac.uk)

6National Centre for Cell Science, Pune and School of Agriculture, Graphic Era Hill University, Dehradun, India(AS: [avinash.nccs@gmail.com](mailto:avinash.nccs@gmail.com) )

7 School of Digital, Technologies, and Arts, Staffordshire University, Stoke-on-Trent, UK (MA: [Md.Asaduzzaman@staffs.ac.uk](mailto:Md.Asaduzzaman@staffs.ac.uk))

8Division 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](mailto:a.zumla@ucl.ac.uk)).

9School of Life Sciences, Faculty of Natural Sciences, Keele University, Keele, Staffordshire, United Kingdom, ST5 5BG (NH: [n.haider@keele.ac.uk](mailto:n.haider@keele.ac.uk)).

**\*Corresponding author:** Dr Najmul Haider PhD, School of Life Sciences, Keele University, Huxley Building, Room 122, Keele, Staffordshire, ST5 5BG, United Kingdom, Email: [n.haider@keele.ac.uk](mailto:n.haider@keele.ac.uk) , Phone **:** [(+44) 01782 734414](tel:+441782734414)

**Abstract (word count: 304, target 300).**

Bangladesh experienced it’s largest and deadliest dengue outbreak by reporting the highest-ever recorded annual cases and deaths caused by dengue virus (DENV) infection in 2023. This study aims to characterize the geographical transmission dynamics of the dengue virus infection in Bangladesh.

We collected daily reported dengue cases, and death data from the Management Information System (MIS) of the Ministry of Health and Family Welfare, Bangladesh, meteorological data from the Bangladesh Meteorological Department for the period 1 Jan – 31 Dec 2023, and district-wise population and geographical data from the Bangladesh Bureau of Statistics. We performed different statistical analyses including a Generalized linear mixed effect model to understand the geographical distribution of dengue cases in Bangladesh.

The number of dengue cases reported in 2023 is 1.3 times higher than the number of reported cases in the past 23 years (320,710 vs 244,246) with two times more deaths than the number of fatalities recorded in the past 23 years (1699 vs. 849). The 2023 outbreak is characterized by an earlier surge of dengue cases with exponential growth in Dhaka city up until the end of July and then an increase in cases outside Dhaka. The districts in the southern part had higher incidence (cases per 100 people) including Manikgong (0.83), Dhaka (0.77), Pirojpur (0.61), Barisal (0.53), and Magura (0.49) as the top five district. Population density of the district (r=0.44, P<0.05) and distance from the capital city Dhaka (r=-0.30, p<0.05) were correlated with district-wise dengue cases. Through, GLMM, the urban: rural population ratio of the district (IRR: 1.03) were temperature (IRR: 1.01) and rainfall (IRR: 1.01) were associated with dengue cases of the district.

The 2023 outbreak shows a geographical shift of the dengue cases from the capital city Dhaka to different districts of Bangladesh with a higher incidence of cases in the southern district of Bangladesh.

**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 respectively 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 (2018-2022): more than 82% of cases (n=202,425) and 69% of deaths (n=550) of last 23 years were reported during this period 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 capital city Dhaka, 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, whereas more than 58% (979 of 1699) deaths were recorded in Dhaka.

*Aedes aegypti,* the primary vector of dengue virus is known for its preference for urban and suburban environments7. Several factors contribute to this affinity for urban areas including the presence of artificial containers, human habitation and blood hosts, microclimate in urban areas, and adaptability 7. On the other hand, *Aedes albopictus*, the second important vector of the dengue virus exhibits a broader habitat range including rural and urban areas8. Other factors that affect the spreading of the dengue virus are urbanization, population density, rainfall and watering distribution systems, and temperature 9. As Bangladesh is recently experienced a country-wide distribution of dengue cases, this is important to understand factors that affect the geographical distribution of dengue cases in Bangladesh. The objective of this study was to characterize the geographical transmission dynamics of dengue virus infection in Bangladesh and to characterize the spreading of dengue virus infection 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 10. 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 23.46, Lon 90.23).

**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 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.

**Incidence by district**

We calculated the cumulative district-wise incidence of dengue cases by taking the annual number of dengue cases of each district divided by the population of the district which is shown as -(The total number of dengue cases in a district in 2023) / Total number of populations of that district) \*100. We then prepared a map of Bangladesh suing district-wise incidence of dengue cases in 2023.

**Statistical Analysis**

We compared the dengue cases and deaths of the year 2023 and previous years (2000-2023), prepared graphs, plots, and maps, and compared these data with meteorological data. We expanded our dataset by incorporating district-wise dengue case data as outcome variables. We further collected district-wise population and geographical data from the Statistical Yearbook Bangladesh 2022 published by the Bangladesh Bureau of Statistics 11 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.

In this study, we employed a generalized linear mixed model (GLMM) to account for associations among variables, enhancing modelling flexibility through the inclusion of random effects 12. This approach accommodates the analysis of non-normally distributed response data with extra-variation (overdispersion) 13. Parameter estimation in GLMMs is challenging due to the integration of random effects in the likelihood function 14. Consequently, our model results are presented as adjusted incidence rate ratios (IRRs), considering dengue deaths, the urban-rural ratio (as an urbanization proxy), population density, and distance from Dhaka, along with corresponding 95% confidence intervals. The components of the GLMM are given below:

Distribution: ~ Negative Binomial (,

~ N (,

Linear predictor:

Link function:

where denotes the number of cases in day i on division j (i = 1, 2, ⋯, 365; j = 1, 2, ⋯, 8), is the linear predictor, is the intercept, is the fixed effect due to day i, and is the random effect due to division j.

(https://link.springer.com/chapter/10.1007/978-3-031-32800-8\_5)

**Results:**

During 2023 (1 Jan to 31 December), a total of 321,179 dengue cases have been reported with 1,705 deaths (case fatality ratio: 0.53%). The number of cases reported in 2023 is 1.3 times higher than the number of reported cases in the past 23 years (321,179 vs 244,246) and two times more deaths than the number of fatalities recorded in the past 23 years (1,705 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)**. Among the dengue cases, 40% were female and 56% were below 30 years of age group. A total of 110,008 cases were reported from the capital City Dhaka including 980 deaths (case-fatality rate: 0.89%) and 211,171 cases were reported from outside Dhaka including 725 deaths (case-fatality ratio of 0.34%).



**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 rainfall of the period 2000-2022. The average rainfall for the period 2000 to 2022 was 1914.74 mm whereas in 2023 total annual rainfall increased to 2162 mm **(Fig 2)**. In 2023, rainfall started earlier in the year with 90 mm of precipitation in March compared to an average of 45 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 26.46 °C for the period 2000 to 2022, the temperature decreased marginally to 27.61 °C in 2023 **(Fig 2)**.



**Fig 2:** The temperatures (°C) and rainfall (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 was the primary outbreak site in 2023 and contributed to more than 50% of the total cases up until July and then cases started to increase outside the Dhaka, where Dhaka division (excluding Dhaka city) and Chittagong division have been among the prominent sites of the outbreak **(Fig 3)**. In May, Dhaka city contributed more than 83% of the total cases in the country which dropped to 23.4% in December. The relative changes of 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).** Bangladesh observed one of the largest festivals of the Muslim-majority country Eid-Ul-Adha on 28th July 2023 and many people travelled from Dhaka to their rural house located outside Dhaka. 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)**. The Sylhet division contributed less than 1% of cases throughout the year.

A graph of different colored lines and numbers

Description automatically generated

**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.

We compared 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 number of people from 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 number of dengue with 113,233 cases, followed by Chittagong (14,200), Barisal (13,603), Manikganj (12,952), and Patuakhali (7,579). On the contrary, 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 981, trailed by Barisal (167), Faridpur (138), Chittagong (106), and Khulna (41) division **(Fig 5)**.

For district-wise cumulative incidence, the districts located southern part of Bangladesh had a higher incidence of dengue cases in 2023. Manikganj a neighbouring district of Dhaka had the highest incidence of dengue with 0.83 cases per 100 people, followed by Dhaka (0.77), Pirojpur (0.61), Barisal (0.53), and Magura (0.49). Conversely, the lowest Dengue cases were recorded in Sunamganj (0), Maulvibazar (0.01), Panchagarh (0.02), Sylhet (0.02), and Thakurgaon (0.02), most of these districts were located **(Fig 5)**.



**Fig 5: A (Left). The distribution of dengue cases in different districts of Bangladesh, 1st Jan 2023 – 31st Dec 2023. B (Right) The incidence of dengue cases in each district in Bangladesh (1st Jan- £1 Dec 2023). A higher incidence of dengue cases is observed in the southern districts of Bangladesh.**

**Correlation:** When compared with monthly dengue cases, a positive correlation was observed between population size and the number of dengue cases (r=0.44, p=<0.001) and deaths (r=0.43, p=<0.001). A similar association is evident in the relationship between population density and 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=-0.32, p=0.011) **(Fig 6)**.



**Fig 6:** The correlation coefficient of dengue cases and deaths in different districts and its 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 GLMM, a statistically significant positive association was identified between the dengue cases and urban and rural population ratio (IRR:1.03, 95% CI: 1.02-1.05), daily average temperature (IRR: 1.01, 95% CI: 1.01-1.02), and daily total rainfall of the division (IRR1.01, 95% CI: 1.01-1.02). Population density and distance from Dhaka exhibited weak negative associations without statistical significance (Table 2).

**Table 2: Factors associated with Dengue cases in different Divisions using a generalized linear mixed model during 1 Jan 2023 and 31 Dec 2023.**

|  |  |  |
| --- | --- | --- |
| **Variables** | **Incidence risk ratio (IRR)** |  |
| **95% Confidence Interval** | **P-value** |
| Urban-rural ratio | 1.03 (1.02 – 1.05) | <0.001 |
| Population density | 0.99 (0.99 - 1.00) | 0.143 |
| Distance from Dhaka (capital city) | 0.99 (0.99 - 1.00) | 0.253 |
| Daily average temperature | 1.01 (1.01 - 1.02) | <0.001 |
| Daily total rainfall | 1.01 (1.01 – 1.02) | <0.001 |
| **Groups Name** | **Variance** | **Standard Deviation** |
| Location (Intercept) | 0.01652 | 0.1285 |
|  |  |  |
| **Akaike information criterion (AIC)** | **Bayesian Information Criterion (BIC)** | **Root Mean Square Error (RMSE)** |
| 24877.9 | 24925.7 | 225.7 |
| **Conditional *R2*** | **Marginal *R2*** | **Intraclass correlation (ICC)** |
| 0.135 | 0.128 | 0.009 |

**Discussion:**

Besides a very high number of dengue cases and deaths, Bangladesh’s 2023 dengue outbreak shows some unique characteristics including i) a geographical shift of cases from inside the capital city to outside Dhaka, ii) a very high case-fatality ratio of dengue cases in capital City Dhaka, iii) early onset and surge of cases in Dhaka followed by spreading of cases across the country iv) geographical spreading of the cases were negatively associated with distance from capital city Dhaka.

The case-fatality rate observed in 2023 is 10 times higher than WHO’s goal to limit the dengue-related CFR below 0.05% 15. 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 (0.53%) which is inflated by a very high fatality rate in the capital city Dhaka (0.88%). 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 16. More than 44% of patients with DENV infection admitted to hospitals in Dhaka city were from outside Dhaka 17. Also, there is a more regular and organized notification of deaths from Dhaka city as compared to other parts of the country where deaths might be underreported specially when occurred in private health care facilities. Bangladesh dengue 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 17 Thus, current surveillance system 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.

Several drivers contributed to the largest outbreak of dengue fever in Bangladesh. First, the dengue serotype -2 (DENV-2) reappeared in Bangladesh after 2018 18. 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) 18. 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) 18. 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.

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 19. 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 20. 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 country17. More than 15 million people left Dhaka and its surrounding cities to celebrate Eid-Al-Adha with their families in rural Bangladesh21. This large movement probably played a role in spreading the DENV throughout the county. People infected with DENV can remain viremic (infectious) for a maximum of 12 days 22. 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 6,23. 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 17. 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 areas24. 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.

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%) 25. 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 22. 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**.**

**Conclusion:**

Bangladesh’s 2023 dengue outbreak is characterized by the early onset and surge of dengue cases in the capital city Dhaka with an earlier rainfall in March (90 mm) and the spreading of the virus during Eid-Al-Adha, the Muslim’s largest religious festival in the country. Although more cases were reported from Outside Dhaka, most deaths were recorded in the capital city Dhaka which might be associated with increased secondary infection due to the introduction of new serotype DENV-2 in the country. Distance from Dhaka city showed an increased risk of a higher number of district-wise cases in Bangladesh. Bangladesh needs short-, medium--, and long-term plans to control or at least alleviate the burden of dengue-related cases and deaths in the country. Besides, planning is essential to address unusual rainfall which extends vector season in the country,

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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% | 23.39% |
| 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% | 21.95% |
| Mymensingh | 7 | 1.80% | 1.79% | 1.39% | 1.25% | 1.61% | 2.68% | 3.16% | 2.65% | 2.02% | 2.29% | 3.14% |
| Chittagong | 140 | 23.95% | 16.07% | 23.61% | 7.91% | 8.11% | 13.36% | 14.98% | 15.13% | 13.22% | 11.24% | 15.36% |
| Khulna | 24 | 4.19% | 4.46% | 3.47% | 0.77% | 1.98% | 3.97% | 6.27% | 10.32% | 15.64% | 19.49% | 16.88% |
| Rajshahi | 7 | 0.60% | 0.89% | 0.69% | 0.10% | 0.45% | 2.33% | 4.32% | 5.52% | 8.60% | 10.49% | 8.16% |
| Rangpur | 2 | 0.60% | 0.89% | 0.69% | 0.10% | 0.47% | 1.85% | 2.40% | 1.68% | 1.53% | 1.13% | 1.57% |
| Barisal | 53 | 16.77% | 12.50% | 8.33% | 3.95% | 4.58% | 11.12% | 11.75% | 13.46% | 12.18% | 10.95% | 9.44% |
| Sylhet | 3 | 0.60% | 0.89% | 0.69% | 0.19% | 0.64% | 0.88% | 0.71% | 0.32% | 0.24% | 0.16% | 0.18% |