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The 2023 Dengue Outbreak in Bangladesh: Serotypes, Causes, and Impact

Md Yasin Ali Parh[1,2], Mst Sharmin Akter Sumy[1,2], Md. Murad Hossain[3*], Nayeem Bin Saifuddin[4], Jannatul Ferdousi Elma[5], Hamid Zarei[6], Md Nazmul Hasan[7]

[1)] *University of Louisville, Louisville, KY, USA*

[2)] *Department of Statistics, Islamic University, Kushtia, Bangladesh*

[3)] *Gopalganj Science and Technology University, Gopalganj, Bangladesh*

[4)] *Dhaka Nursing College, Dhaka, Bangladesh*

[5)] *Kumudini Nursing College, Mirzapur, Tangail, Bangladesh*

[6)] *University of Louisville, Louisville, KY, USA*

[7)] *University of Saskatchewan, Saskatoon, SK, Canada*

Abstract: The rapid spread of the mosquito-borne fever, dengue, is a growing public health concern in Bangladesh. The nation experienced its worst dengue outbreak in 2023. This study aims to present an overview of the 2023 dengue situation in Bangladesh. We utilized monthly reported data on dengue cases and dengue-related deaths obtained from the Bangladesh Institute of Epidemiology, Disease Control and Research (IEDCR).

Keywords: Dengue outbreaks, cases, deaths, CFR, Public health crisis.

1. INTRODUCTION

Dengue virus (DENV) infection remains a significant global public health problem that is brought on by four closely related serotypes of the virus (DENV 1- 4) and it is most commonly found in urban and semi- urban areas of tropical and subtropical climates [33]. According to the World Health Organization (WHO), dengue fever is now endemic in more than 100 nations [8]. In 2023, and as of the end of July, over three million cases and over 1500 dengue-related deaths have been reported globally [12]. Furthermore, every year, an estimated 400 million individuals become infected with the dengue virus, 100 million become sick, and 21,000 die as a result of dengue [8]. A minor fever to the potentially fatal dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS) can be brought on by any of the four serotypes of DENV infection [23]. Infection with one serotype confers lifetime immunity to that serotype but does not provide long-term protection against the other three serotypes [28, 21]. Dengue has a wide spectrum of clinical signs and is usually accompanied by hematological changes such as leukopenia and thrombocytopenia in mild cases and Vascular alterations, including vasodilation and increased permeability. DENV infection contributes to plasma leakage, hemorrhage, or organ impairment, such as liver damage [22, 34]. Evidence suggests that severe dengue patients have systolic and diastolic cardiac dysfunction as a result of the septum and right ventricular wall injury [35]. While clinical manifestations are typically modest, a potentially fatal complication known as severe dengue can arise and is the leading cause of hospitalization and mortality of patients [26, 32].

Many factors are contributing to increase the dengue transmission intensity. Increased population, international travel, worldwide trade, uncontrolled urbanization, mosquito

* Corresponding author: murad.stat@gstu.edu.bd

migration, climate and environmental changes, human host immunity, and virus genotype are regarded to be key reasons for increasing the intensity of dengue virus transmission [7,9,13,20,24,27,31].

The El Nin˜o weather phenomenon, anticipated to intensify the already rising temperatures in Asia, is also projected to heighten the prevalence of mosquito-borne diseases such as dengue [4].

Dengue fever outbreak control is difficult in tropical settings, where rising temperatures can make longer the length of the mosquito sea- son and provide more time for dengue transmission. Bangladesh, like other Southeast Asian (SE) countries, with a population of approximately 165 million, has become a perfect environment for the dengue vector, resulting in an increase in dengue transmission since the first outbreak in 2000 due to its proximity to the equator and subtropical/tropical temperature [25].

Dengue fever has spread to 64 districts in Bangladesh, and public health experts believe that the situation is worse now and posing a substantial risk to a large number of individuals. Between 2012 and 2019, the most dengue cases were reported in Dhaka, Bangladesh's capital and most populous city, with a population of almost 16 million people [5, 29].

Last year the number of dengue infections has soared more, especially in the capital, Dhaka. Hospitals are overwhelmed by the outbreak. The dengue outbreak in Bangladesh has taken a concerning turn this year, with an alarming spike in cases and fatalities. According to a Directorate General of Health Services (DGHS) survey of 50 dengue patients, women are more likely than men to die from dengue (62% versus 38%, respectively). Additionally, it demonstrates that dengue killed the majority of individuals between the ages of 19 and 50 [18]. There is evidence of a potential gender and age-specific difference in morbidity and death, which may point to more serious infections in specific age groups. Even though only a few hospitals were reported in the majority of the research, and the sample sizes were modest, these studies may nevertheless offer useful data on the distribution of age, sex, and other demographic characteristics.

A safe and effective dengue vaccine must be available and should have strong and long-lived protection against all four serotypes to avoid making a person particularly vulnerable to dengue disease. Furthermore, community awareness and health care prevention are critically important in disease prevention [3].

Inadequate health care infrastructure, lack of outbreak planning, and awareness of dengue infection may result in public health crises if suitable prevention techniques are not taken ahead of time. It is an urgent need to reveal the reasons for mosquito behavior changes, possible reasons for dengue outbreaks, and gender and age-specific differences in morbidity. As a result, the purpose of this study was to investigate the prevalence of dengue and precise accounting of the number of cases, mortality rates, dominating serotypes, epidemiology, and clinical presentation of dengue virus in order to present a comprehensive picture of the dengue pandemic in Bangladesh, which could benefit in the diagnosis and control the future outbreaks.

1. METHODS

1.1. Data Collection

Data was compiled from the national database, which had released the con- firmed dengue cases and related deaths through a government press release from the Directorate General of Health Services (DGHS), Ministry of Health and Family Welfare, Bangladesh. The website https://old.dghs.gov.bd/index. php/bd/, from which we collected all the released data. The dataset included all officially reported dengue cases and dengue-related deaths compiled by DGHS/IEDCR from January 1, 2023 to December 31, 2023. Monthly reports covering this full one-year period were extracted and used for all analyses.

1.2. Data Source and Validation

All dengue-related data were retrieved from the Directorate General of Health Services (DGHS) official press releases and the Bangladesh Institute of Epidemiology, Disease Control and Research (IEDCR). These data undergo internal verification at DGHS before public release, including validation of case counts reported from government and private hospitals. To ensure reliability, we cross-checked the monthly cumulative data with daily situation reports published by DGHS and confirmed consistency of case and death counts across releases. We also screened the dataset for anomalies, duplicate entries, inconsistencies in cumulative curves, and missing values; no significant missingness was identified.

1.3. Statistical Analysis

We conducted descriptive statistical analyses to summarize dengue cases, deaths, and case fatality rates (CFR) by month, age group, gender, and geographic location. Categorical variables (e.g., gender differences in CFR and case distribution across regions) were compared using the Chi-square test. When comparing continuous variables, we used independent sample t-tests or the Mann–Whitney U test when normality assumptions were not met. Age-specific and gender-specific CFR differences were evaluated with proportion tests. Time-series trends (weekly and monthly fluctuations) were assessed through graphical visualization and percentage change calculations. All analyses were performed using standard statistical software (e.g., R or SPSS), and a p-value < 0.05 was considered statistically significant.

2. RESULTS AND ANALYSIS

In this section we will discuss our results and analysis through a subsection of brief history of dengue outbreak in Bangladesh

2.1. A Brief History of Dengue Outbreak in Bangladesh

Dengue was first recorded in the 1960s in Bangladesh (East Pakistan) and was known as “Dacca fever” [30]. From that time dengue fever has become an endemic disease, infecting thousands of people and lowering people’s quality of life. Dengue fever occurrences documented every year since 2000 with new cases being reported every day. In 2019, Bangladesh saw the greatest number of dengue infections (101,354 cases) and 179 people died [17]. Due to excessive rainfall, water-logging, flooding, temperature rises, and odd shifts in the country’s conventional seasons, Bangladesh’s climate conditions are becoming more suitable for the transmission of dengue and other vector-borne diseases such as malaria and chikungunya [2]. An abnormally lengthy wet season, and resistance to pesticides which are used by local authorities considered major drivers of that outbreak [19]. Based on accessible hospital-based surveillance data, seven outbreaks with over 5,000 hospitalized cases were recorded in Dhaka City between 2000 and 2022. A significant segment of Bangladesh’s populace opts to reside in urban areas due to the potential for improved earnings, access to quality education, and better overall amenities. The dengue outbreak in Dhaka in 2019 marked the most severe instance since dengue outbreaks first appeared in Bangladesh in the late 1990s [16]. This epidemic was followed by a significant outbreak in 2021 (28,429 cases and 85 deaths), the real size of which is thought to be hidden by the COVID-19 pandemic

(delta onslaught). Another large outbreak occurred (61,732 cases, 281 deaths) in 2022. Up to 2021, Dhaka remained the epicenter of all large outbreaks. Later on, all the districts in Bangladesh experienced a significant outbreak with a large number of cases and death rates. Even though dengue is common in Bangladesh, the most recent outbreak (2023) is exceptional in terms of the number of cases and deaths, seasonality, and the abrupt early upsurge.
Fig. 1 presents a clear picture of dengue-related cases from 2014 to 2023. The majority of confirmed dengue fever cases occurred in the latter half of the year, as depicted by the graph.

As of August 3, in 2023, the death toll exceeded that of previous years, and by August 21, the number of hospitalizations had surpassed the highest recorded during the 2019 outbreak [11]. In September 2023, 79,598 confirmed cases of dengue fever were the highest monthly total on record. Also, in September 2023, 25.0% of cases and 23.2% of deaths of total cases and deaths of this year were reported. The reported number of dengue cases and deaths this year so far is the highest ever recorded in the country. The subsequent highest dengue confirmation was in August 2019 (confirmed cases 52,636). In 2019, 101,354 cases of dengue fever were confirmed, with nearly 98% of cases occurring between July and December. It's noteworthy that Bangladesh's death rate has somewhat grown in recent years. Similar to past years, the epidemic commenced during the summer months (April–May), proliferated, and escalated across the entire nation during the monsoon season (July–August) [33].

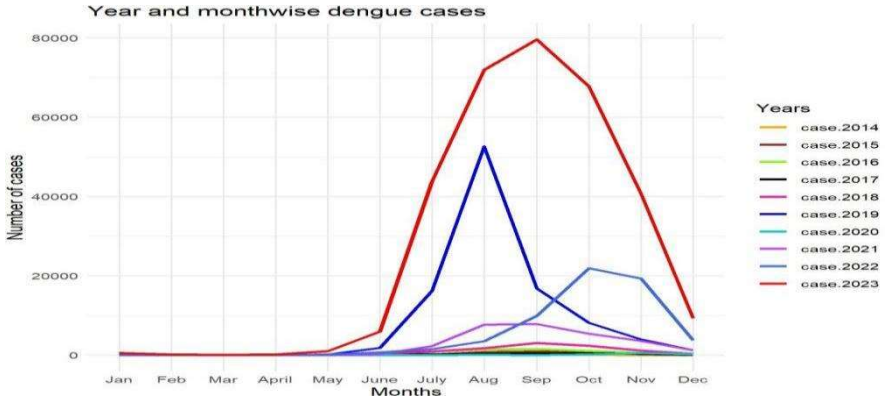


Fig. 1. Year and month-wise dengue reporting in 2023

Fig. 2 provides a distinct visualization of the weekly variations in dengue cases throughout the year, 2023. In Dhaka division, the surge in cases began during epidemic week 17 (23-29 April 2023, 27 new cases in Dhaka and 14 cases outside of Dhaka), while all eight divisions experienced an uptick from epidemic week 26 (25 June to 1 July 2023, 1409, cases) onward.

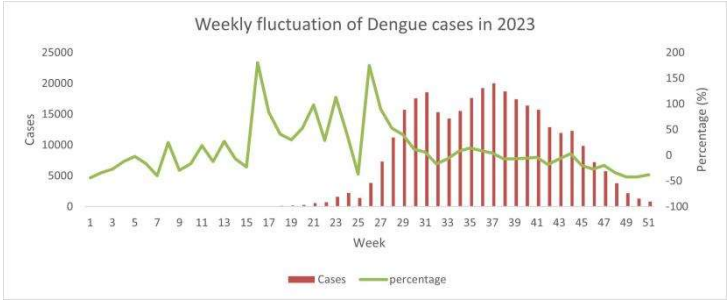


Fig. 2. Weekly fluctuation of Dengue cases in 2023

Fig. 3 shows the monthly Dengue CFR of 2019 and from 2021 to 2023. The picture shows that although the death rate in April of 2023 is low com- pared to the death rate in April of 2019, and for other months of 2023, death rates are higher compared to the other months of different years. Also, the figure shows that the start of May has the highest concentration of dengue- reported deaths for all different years. In 2023, although the CFR was very high in February but March onwards, it has just reached a steady level with a high CFR for the next several months. It indicates that last year's outbreak is exceptional due to the high caseload, high fatality rate, seasonality, and abrupt early spike. The dengue outbreak is getting worse due to altered weather patterns brought on by climate change. Less rainfall does not always stop the spread of dengue, even in Bangladesh when the monsoon seasons end, and the weather turns dry. The mix of temperature, humidity, and rainfall determines the ideal circumstances for Aedes mosquitoes to flourish.

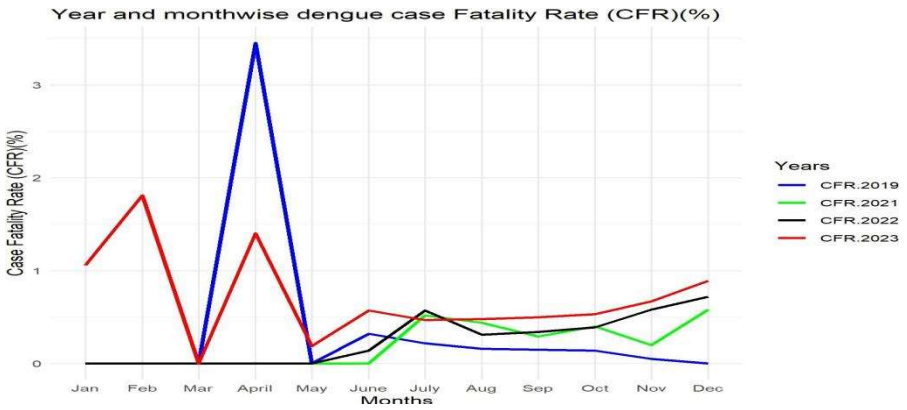


Fig. 3. Year and month-wise Case Fatality Rates (CFR) of 2019, and from 2021 to 2023

Analyses of data from inpatient records and geographic coordinates of residence locations between 01 January and 31 December of 2023 highlighted two important findings that require further epidemic investigation: First, approximately half of the cases (n=110,008; 34% of confirmed dengue cases) and deaths (n=980; 57% of dengue-related deaths) were recorded in the capital city Dhaka raising concern about the high density of DENV patients in the proximity of the hospitals (Fig. 4(a)). Dhaka bears the brunt of the outbreak and serves as the epicenter, with over half of the reported cases originating in this mega-city [6].

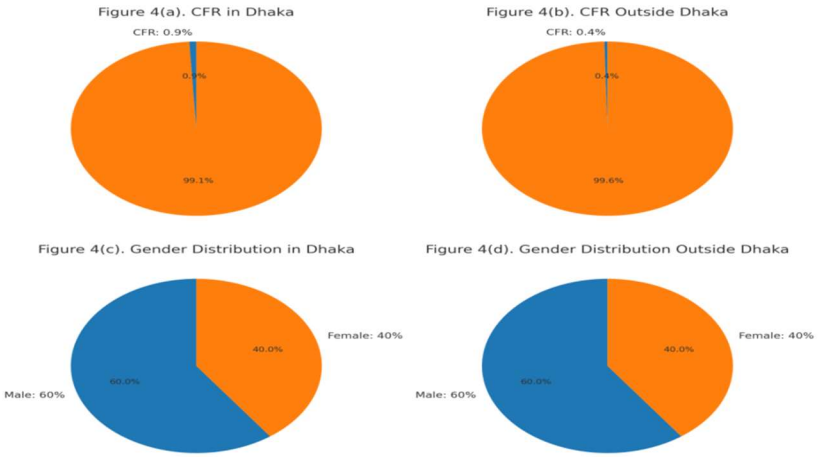


Fig. 4. (a) Case Fatality Rate CFR (%) of patients living in Dhaka city and outside of Dhaka city (b) Gender wise Case Fatality Rate (%) (c) Percentage of gender wise cases in Dhaka city (d) Percentage of gender wise cases in outside of Dhaka city

Second, although the percentage of female patients in Dhaka and outside of Dhaka city are less compared to male patients, the overall CFR for female patients (CFR: 0.8) is higher all over the country compared to male patients (CFR: 0.4) (Figure 4(b)). The percentage of gender wise dengue cases in Dhaka and outside of Dhaka are shown in figure 4(c & d). A notable prevalence of males was observed, constituting 60% of cases in both Dhaka and outside of Dhaka city. Women may have preferred to stay at home for longer periods and delay visiting a doctor, these could be the possible reasons for high CFR. In every study, the percentage of male cases was approximately twice as high as that of female cases and the male-to-female ratio reached 2.7 [1]. Hospital-based studies reveal that male patients are more common in developing nations like Bangladesh, this disparity may be the result of case selection bias. Another factor can be the cultural fact, as Asian women are typically wearing long dresses.

Gender wise dengue cases for different age groups in Dhaka and outside of Dhaka are shown in Fig. 5 The distribution of age among individuals infected outside of Dhaka city reveals that the majority of cases (46%) occurred in the 16 to 35 years age group, whereas the age group above 71 years constituted the smallest proportion (< 2%). In terms of gender, males

exhibited higher infection rates than females across all age groups outside of Dhaka city. Likewise, the breakdown of age among infected individuals in Dhaka city shows that the largest percentage of cases (50%) occurred in the 16 to 35 years age group, while the age group above 71 years constituted the smallest fraction (< 2%). Regarding gender, males demonstrated elevated infection rates compared to females across all age groups in Dhaka city.

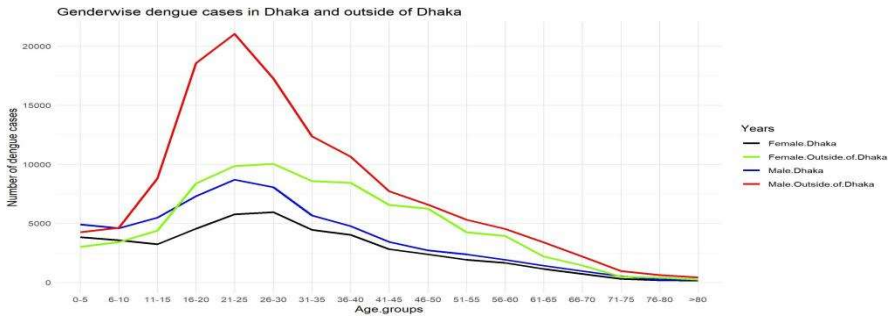


Fig. 5. Gender wise dengue cases in Dhaka and outside of Dhaka

We discovered indications of a potential age-specific variation in CFR nationwide, suggesting more severe infections in older age groups of male patients (⩾ 76 years with CF R : 2.9) compared to female patients (⩾ 76 years with CF R : 1.8). This information is illustrated in Table 1 and Fig. 6. The older age group recorded a higher CFR compared to the younger age group. In 2023, more than 57% of confirmed cases were adults, with the greatest age range for cases being between 16 and 40 years old. Approximately 29% of all dengue cases in Bangladesh are observed in children and youth under the age of 20. Children frequently engage in outdoor activities without wearing long-sleeved clothing, and a significant number do not utilize mosquito nets during sleep at night. Children under the age of five, in particular, face an elevated risk of experiencing severe symptoms such as dehydration and shock resulting from dengue.

Table 1.1. Distribution and predominant DENV serotypes in different districts of Bangladesh

Age groups	Number of Female Cases	Number of Male Cases	Number of Female deaths	Number of Male deaths	$CFR = \frac{Death}{Cases} \times 100$ $for\ Female$	$CFR = \frac{Death}{Cases} \times 100$ $for\ Male$
0-5	6854	9165	35	31	0.51	0.34
6-10	6990	9219	37	21	0.53	0.23
11-15	7630	14299	23	21	0.3	0.15
16-20	12930	25865	44	56	0.34	0.22
21-25	15625	29718	82	43	0.52	0.14
26-30	15985	25299	90	58	0.56	0.23
31-35	13015	18045	116	39	0.89	0.22
36-40	12465	15419	107	58	0.86	0.38
41-45	9375	11142	79	54	0.84	0.48
46-50	8623	9309	84	55	0.97	0.59
51-55	6183	7676	57	55	0.92	0.72
56-60	5602	6463	78	56	1.39	0.87
61-65	3334	4827	51	67	1.53	1.39
66-70	2155	3161	38	49	1.76	1.55
71-75	802	1481	21	28	2.62	1.89
76-80	588	878	8	18	1.36	2.05
>80	413	644	10	26	2.42	4.04

Males between 21 to 25 years have been seen to be more affected whereas more female patients are affected at age between 26 to 30 years old.

In 2023, more than 57% of deaths were adults aged 21-50 years old. People 30 years old accounted for 44% of deaths in 2023. On further analysis, the overall CFR is higher in females than in males (male CFR: 0.4, female CFR: 0.7). Females have around three times higher CFR than males among those aged 16-40 years (male CFR: 0.2, female CFR: 0.6). In the majority

of age categories, women exhibited a higher number of reported deaths compared to men. This discrepancy could be attributed to gender related differences in health-seeking patterns, suggesting that men may have greater accessibility to healthcare resources, while women of working age might seek healthcare less frequently than their male counterparts.

In Bangladesh, dengue primarily impacted young adults. More than 80% of infections during the initial outbreak in 2000 were adults (> 18 years old), with the greatest age range for cases being between 18 and 33 [25].

In addition, the majority (62%) of confirmed cases in the 2002 outbreak were in the 16–30 age range, with a mean age of 29 [16]. Additionally, the majority of cases in 2016 (21-40; 55%), 2018 (15-29; 65%), and 2019 (21-40; 50%) outbreaks were older adolescents and young adults [16]. During the 2019 outbreak, a hospital-based investigation indicated that the majority (46.1%) of the kids were in the 10 to 14 age range, with a mean age of 8.8 years [19].

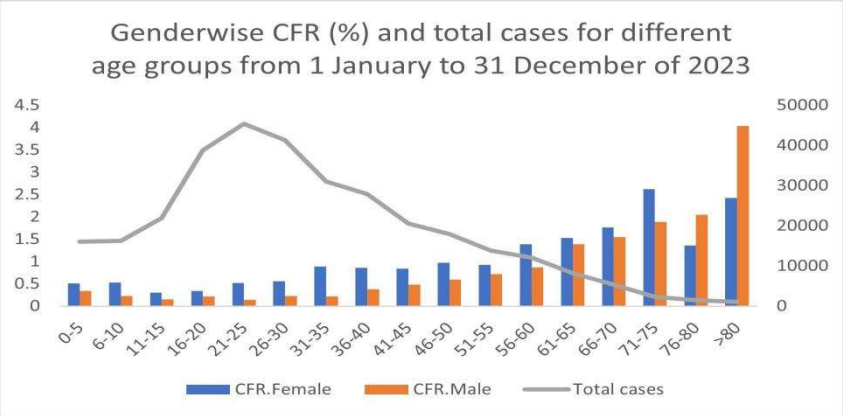
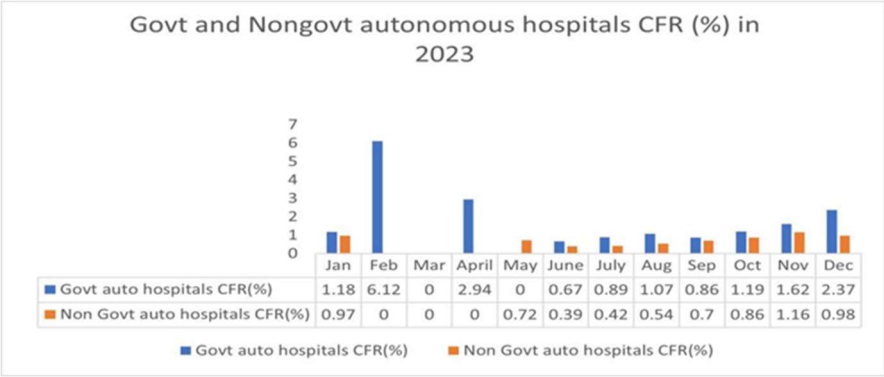


Fig. 6. Gender wise CFR (%) and total cases for different age groups in 2023

According to the data presented in Fig. 7, the current dengue surveil- lance of government and non-government autonomous hospitals reveals that throughout the year 2023, CFR is consistently higher in government autonomous hospitals compared to their non-government counterparts. Government hospitals are free of charge and impoverished people tend to visit more. Private hospitals typically charge far more for supportive care, which is beyond reach for most Bangladeshis. By July 25, cases requiring hospitalization were documented in all districts, and the count of hospitalizations outside Dhaka city exceeded that within the capital on August 14. Government hospital visit to impoverished households has a disproportionate impact on high CFR. Government hospitals have insufficient risk management, lack of necessary care, testing kits, blood bags, platelet kits, staff, and beds, and the surveillance mechanisms are not up to the task of handling the growing dengue hazards.



	Jan	Feb	Mar	April	May	June	July	Aug	Sep	Oct	Nov	Dec
Govt auto hospitals CFR(%)	1.18	6.12	0	2.94	0	0.67	0.89	1.07	0.86	1.19	1.62	2.37
Non Govt auto hospitals CFR(%)	0.97	0	0	0	0.72	0.39	0.42	0.54	0.7	0.86	1.16	0.98

Fig. 7. Case Fatality Rate (CFR%) in Government and Non-Government Autonomous Hospitals in Bangladesh, 2023

Fig. 8 reported the percentage of the top 10 districts across the country. Dhaka city corporation stands out as the most severely affected area within Dhaka division, contributing to 35.3% of cases and 57.8% of deaths. Dhaka city recorded 63% (n = 41,321) of the total cases and was one of the most affected regions in 2022. In 2023, Dhaka city experienced its highest temperatures in six decades, characterized by an unusually hot spring and subsequent heavy monsoon rains. Even small amounts of stagnant water create an ideal breeding environment for mosquitoes, and the rainy season is still ongoing. Other impacted districts include Chattogram (4.42% of cases), Manikganj (4.03% cases), Barishal (4.24% cases), Faridpur (2.34% cases), Gazipur (2.26% cases), Lakshmipur (2.16% cases), Khulna (2.13% cases), Patuakhali (2.36% cases), and Pirojpur (2.29% cases).

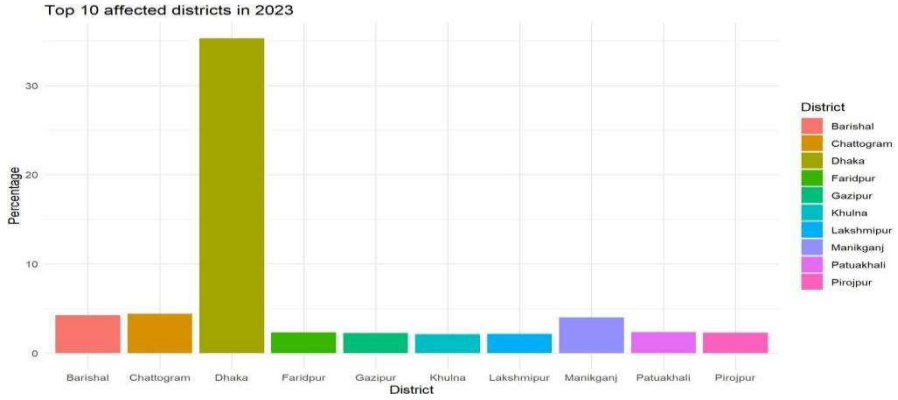


Fig. 8. Top 10 affected districts in 2023

The important question is whether Bangladesh is ready to combat widespread outbreaks of dengue. Bangladesh is currently experiencing its biggest dengue fever outbreak on record, with overflowing patients in hospitals and an increasing number of illnesses and deaths. The recent outbreaks are found to be dominated by serotypes DENV-2 and DENV-3, which have played a major role in increasing clinical presentation severity. The expansion of dengue outbreaks and DENV transmission in many geographic locations of Bangladesh is impending due to the fast and unplanned urbanization, environmental suitability of vector adaption, unconsciousness of people, lack of healthcare facilities, and so on. The dengue outbreak in Bangladesh in 2023 serves as a reminder to pay attention to controlling the dengue epidemic in Bangladesh. In the context of the pandemic our recommendations are as follows,

(a)Cross-infection with different variants increases the risk of complications and fatality, even though a patient does become immune to a particular variant after contracting it. Since the signs of secondary infections change, they suffer shock syndrome or severe dengue, and more deaths are being caused by delayed hospital admissions. Older people and people with neutralizing antibodies to 2 DENV serotypes have a higher likelihood of secondary or tertiary dengue infection and that contributes disproportionately more to DENV transmission [14]. It is necessary to conduct public health campaigns to educate the population about the risks of cross-infection and the importance of seeking medical care promptly. Emphasize the changing signs and symptoms of secondary infections to encourage early recognition and intervention.

(b)Enhancements should be made to the community's efforts to eradicate mosquito breeding areas, which are spearheaded by local leaders and council members as well as voluntary mosquito control groups. From the pattern of this year's hit February is the best time to begin mosquito control measures in Bangladesh. Although dengue vaccinations are finally on the market [10], in order to fully understand their potential to prevent DENV transmission and lower dengue-related morbidity and mortality, field research and controlled trials are needed to assess the vaccines' efficacy and safety.

(c)Bangladesh's main city of Dhaka serves as the focal hub for the management of specialized health care. According to recent data, almost 44% of patients admitted to Dhaka's hospitals came from outside the city [15]. There is a need to expand specialized

healthcare services to other regions of Bangladesh. This can help alleviate the burden on Dhaka's healthcare infrastructure and ensure better access to care for people living in rural areas or smaller towns. In Dhaka, there was a severe lack of electrolytes in both hospitals and pharmacies. Strengthen the supply chain for essential medical supplies, including electrolytes, to ensure consistent availability in hospitals and pharmacies in Dhaka.

(d)Community education, community involvement in risk reduction, and the fortification of preventative measures are all necessary at the community level. People should sleep under insecticide-treated bed nets. The cost of bed nets and insecticides should be reduced. The complete picture of Bangladesh's dengue outbreak is not entirely captured by this constrained surveillance system. It is necessary to conduct proactive nationwide geographic-based surveillance that gathers clinical, demographic, and socioeconomic data to better understand the characteristics of DENV transmission hot-spots as well as the disparities in morbidity and mortality related to age and gender.

2.2. Gender Differences in Morbidity and Mortality

The higher case fatality rate (CFR) among women observed in 2023 may reflect several underlying socio-cultural and economic factors that influence health outcomes in Bangladesh. Evidence suggests that women often delay seeking medical attention due to household responsibilities, reduced mobility, and cultural expectations that prioritize caregiving roles over personal health needs. Financial dependency on male family members may further restrict timely access to healthcare, particularly in rural areas where out-of-pocket expenses represent a significant barrier. In addition, sociocultural norms may prevent women from traveling alone to healthcare facilities, contributing to delayed diagnosis and treatment. These factors collectively may explain the higher CFR observed among women, despite their lower proportion of total reported cases. Biological differences in immune response and comorbidities may also play a role, although additional research is needed to confirm this.

2.3. Potential Drivers Behind the 2023 Dengue Surge

The unprecedented increase in dengue incidence in 2023 is likely the result of multiple interacting factors. Climate change has altered Bangladesh's temperature and rainfall patterns, creating highly favorable environmental conditions for Aedes mosquito breeding. The country experienced unusually high temperatures early in the year, followed by heavy monsoon rainfall, both of which extend the mosquito breeding season and increase vector density. Urbanization also played a substantial role: rapid, unplanned expansion of densely populated cities such as Dhaka has led to overcrowding, poor waste management, and stagnant water accumulation—ideal conditions for Aedes proliferation.

Another major driver of the outbreak was the circulation of more virulent and highly transmissible DENV serotypes, particularly DENV-2 and DENV-3, which have historically been linked to more severe clinical outcomes. Serotype switching and secondary infections may have contributed to the severity of the outbreak, as individuals previously exposed to one serotype are at increased risk of severe disease upon infection with another. Additionally, increased human mobility, population density, and inadequate vector control activities during critical pre-monsoon months further amplified the outbreak's magnitude.

3. CONCLUSIONS AND FUTURE CAUTIONS

In 2023, Bangladesh experienced the highest dengue-related mortality ever recorded, marking a critical point in the nation's public health history. Over the past two decades, there has been a cyclical shift in the circulating DENV serotypes, with all four serotypes (DENV-1 to DENV-4) detected during recent outbreaks, contributing to increased disease severity. The epidemiological pattern of dengue has shifted toward more frequent and severe outbreaks since the first major event in 2000. Several factors contribute to the rising burden of dengue in

Bangladesh, including high population density, rapid and unplanned urbanization, inadequate housing and waste management systems, and favorable climatic conditions for mosquito breeding. These conditions underscore the urgency for both immediate and sustained interventions. To effectively reduce the risk of future outbreaks, year-round efforts to eliminate mosquito breeding sites and destroy Aedes habitats must be intensified. Strong government policies that support vector control, urban planning, and waste management are essential. Furthermore, community engagement plays a vital role in prevention strategies. Raising public awareness through community healthcare workers, local campaigns, social media, and television can empower citizens to take proactive measures at the household and neighborhood levels. Lastly, continuous surveillance to detect the circulating serotypes, monitor clinical manifestations, and understand underlying risk factors is crucial for informed public health planning. A coordinated effort involving government bodies, healthcare institutions, and the general public is imperative to control dengue and minimize its impact in the coming years.

DECLARATIONS

The authors declare that they have no competing interests.

Author Contribution Declaration

MYAP and MSAS contributed to the design of the study, analyzed data, and drafted the manuscript. MMH, NBS, JFE, and HZ interpreted results, contributed to the reviewing of the manuscript, and took the responsibility to check the accuracy of the data analysis. MYAP, MSAS, and NBS provided a critical review of the manuscript.

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