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Editorial

Bangladesh's 2023 Dengue outbreak – age/gender-related disparity in morbidity and mortality and geographic variability of epidemic burdens

Bangladesh is currently grappling to control its most devastating dengue fever outbreak recorded since the dengue virus (DENV) reappeared in the country in 2000 [1–3]. Although dengue is endemic in Bangladesh, the current dengue surge is unusual in terms of case burden and mortality, seasonality, and the early sharp increase [1]. Between 1 January and 25 August 2023, a total of 110,224 DENV infections including 528 deaths (case fatality ratio [CFR]: 0.48%) were recorded [2]. The reported number of dengue cases and deaths this year so far is already the highest ever recorded in the country, while the numbers are continuing to rise [1–3]. The Bangladesh Ministry of Health and Family Welfare's Management Information System (MIS) provides daily reports on cases, deaths, and the district-wise distribution of DENV infections [2]. Analyses of data from inpatient records and geographic coordinates of residence locations between 1 January and 17 August 2023 highlight four important findings that require further epidemic investigation: *First*, approximately half of the cases (n=52,656) were recorded in the capital city Dhaka, and 86% of them were located within a 2-km radius of hospitals, raising concern about the high density of DENV patients in the proximity of the hospitals (Fig. 1). *Second*, although 62% of the cases are males, 58% of the deaths are females indicating a higher risk of mortality among females. *Third*, we identified a possible age-specific disparity in morbidity and mortality indicating more severe infections in the older age group. People ≥30 years old accounted for 38% of cases and 64% of deaths in 2023. *Fourth,* out of 528 deaths, 391 (74%) were recorded among the patients hospitalized in the capital city, Dhaka (Fig. 2).

Currently, Dhaka accounts for approximately 48% (n=52,656) of reported dengue cases and 74% (n=391) of deaths (Fig. 2), showing a higher CFR of 0.74% compared to that of 0.24% in the rest of the country, while the percentage distribution of cases had changed over time. Initially, 76% (n=6,014) of cases were reported from Dhaka up until 28 June when Eid-al-Adha was celebrated by the Muslims in the country. To celebrate the festival, people left the capital city for rural family homes. This probably allowed the spread of DENV from Dhaka to the rest of the country. The reason for more fatal outcomes of dengue in female patients needs further study. The median age of infected males and females are similar, at 25 years and 26 years respectively. Compared to females, males spend more time outdoors, especially during the dawn and dusk, when *Aedes* mosquitoes remain active [3]. Furthermore, males are often earners and decision-makers of the families in Bangladesh, and are more likely to get admitted to the hospital than their female counterparts. It may be that only a small fraction of females who have severe dengue are hospitalized rendering a lower denominator for the gender among admitted patients. Vitamin D deficiency is more frequent in females than males in Bangladesh [4] due to less exposure to sunlight, which might be associated with susceptibility to severe disease. People living in dengue-endemic countries experience a higher cumulative lifetime exposure to DENV and thus older people have a higher likelihood of secondary (when infected with 2nd serotype) or tertiary dengue infection (when infected with a third serotype) which can lead to more fatal outcomes.

The prevention and control of dengue depends on effective mosquito control measures [3,5–7]. The mosquito vectors for DENV, *Aedes aegypti* and *Aedes albopictus*, have a short flying range of 500-750m, which breed with the dispersal of eggs within 840 m radius [8]. People with dengue remain viremic for up to a maximum of 12 days [5]. With a concentration of DENV, hospitals treating dengue patients may serve as reservoirs setting up cycles of DENV transmission to people living in hospitals and surrounding areas. Living close to hospitals had been identified as a risk factor for DENV infection [9] and might be associated with a dense population around developed areas, construction sites, and catchment areas of the hospitals. Control of mosquito breeding sites around hospitals should be a priority to reduce hospital-associated transmission of DENV. Emphasis should be given to reducing the mosquito bites of DENV-infected patients by improving bed-net for the DENV-infected patients receiving medical care at hospitals or in the communities.

The ongoing outbreak reveals major gaps in surveillance and early warning systems, data collection, and analyses, and highlights the importance of health service development and conduct of priority epidemiological research. The current Dengue surveillance is based on 20 public and 57 private hospitals in Dhaka and 1-2 main hospitals from each district outside Dhaka [2]. This represents only a small fraction (~5%) of the total number of hospitals in the country. This limited surveillance system does not fully capture the overall picture of the dengue outbreak in Bangladesh. Proactive nationwide geographic-based surveillance with the collection of clinical, demographic, and socioeconomic data is required to better understand age and gender-related disparity in morbidity and mortality, and the characteristics of DENV transmission hotspots. En-

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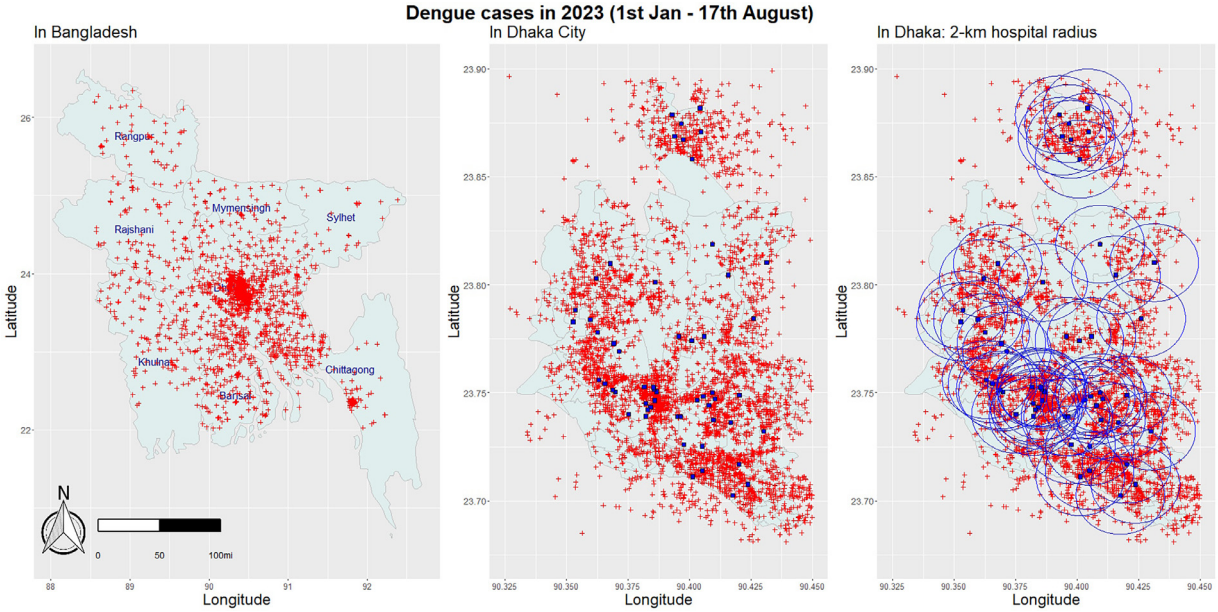

Figure 1. Geographical distribution of dengue cases in Bangladesh: 1 January – 17 August 2023. GPS coordinates of patients' addresses recorded in the hospital registration were extracted using Google Sheet's add-ons 'Geocode by Awesome Table'. More than 48% of dengue cases were recorded in the capital city Dhaka and 86% of the cases in Dhaka city were located within a 2 km radius of the 77 hospitals included in the dengue surveillance system. (Data source: Management Information System, Ministry of Health and Family Welfare, Bangladesh [2]).

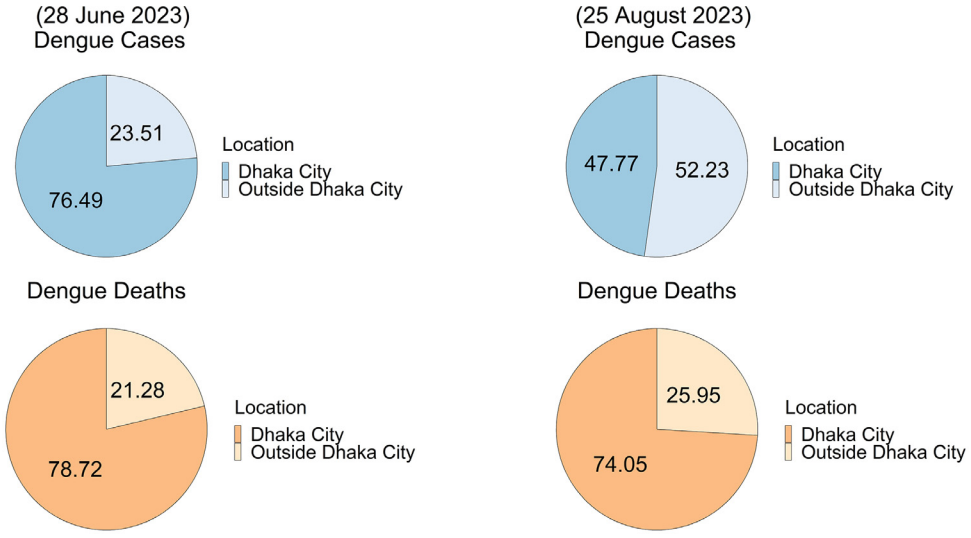

Figure 2. Comparison of proportion of Dengue cases and deaths reported from Dhaka and from outside Dhaka on 28th June (Eid-Al-Adha festival) and on 25th August 2023. Although the percentage of cases changes over time (76% vs. 48%. $P<0.05$) in Dhaka city, the percentage of deaths remains similar over time (78% vs. 74%). (Data source: Management Information System, Ministry of Health and Family Welfare, Bangladesh [2])

tomological surveillance is needed to assess the breeding potential of *Aedes* mosquitoes in environmental containers as well as to monitor insecticide resistance to help inform insecticide-based interventions [1]. Case surveillance should continue to be enhanced in all affected areas and across the country.

In Bangladesh, specialized health care management is centralized in the country's capital city Dhaka. Current data shows that more than 44% of the patients admitted to hospitals in Dhaka had traveled from outside Dhaka city (Fig. 1). More than 80% of people living in the capital city are exposed to the DENV in their lifetime [10]. All four serotypes of the dengue virus have been recorded in Bangladesh at different times since 2000. In 2023, DENV-2 became a predominant serotype (51%) along with DENV-3 (44%) [1] and hospitals were overwhelmed with patients with Dengue [11]. There was an acute shortage of electrolytes in the hospitals and pharmacies in Dhaka [11]. All these factors could have contributed to suboptimal management and increased mortality of severe dengue patients [11]. The health systems in other Southeast and South Asian countries also have a similar structure with a high dependency on the capital or larger cities. Decentralizing healthcare facilities with proactive community education and full engagement is the key to optimizing outbreak management and this should be a mandatory long-term objective for the Bangladesh government.

On a community level, there's the need for community education, community engagement for risk reduction, and the strengthening of prevention measures. Insecticide-treated bednets offer good protection to people against mosquito bites while sleeping as has been highlighted recently for malaria [7]. However, the economic cost of these measures per household makes it unlikely that they will be used unless these are provided free of charge. Recent

World Bank support for Bangladesh is encouraging [12] and the provision of free bednets and insecticides would be prudent.

Mosquito control is challenging even in countries that have functioning mosquito control programs. There are several promising vector-control programs that dengue endemic countries like Bangladesh might consider implementing in the short, medium and long term [13]. Vector control activities should focus on all areas where there is a risk of human-vector contact such as the place of residence, workplaces, schools, and hospitals. WHO promotes a strategic approach known as Integrated Vector Management (IVM) [13] which should be enhanced to remove potential breeding sites, reduce vector populations, and minimize individual exposure. This should involve vector control strategies for both mosquito larvae and adults such as source reduction, especially of water storage practices, covering, draining, and cleaning household water storage containers on a weekly basis; larvicide in non-potable water using WHO-prequalified larvicides at correct dosages; distribution of insecticide-treated nets (ITNs) for fever/dengue inpatients to contain the spread of the virus from health facilities; as well as strategies for protecting people and households. Indoor space spraying (fogging) is another approach for rapid containment of dengue-infected mosquitoes but may be challenging to deliver in densely populated areas such as camps.

Another promising intervention is the Wolbachia-mediated mosquito control program initiated by the World Mosquito Program [14]. The use of Wolbachia in Brazil, Indonesia, Viet Nam, and Australia resulted in a significant drop in dengue cases in intervention sites of over 69% [15].

Biological larvicides using *Bacillus thuringiensis vs. israelensis* (B.T.I) is another encouraging mosquito control intervention. Eradication of mosquito breeding sites by community initiatives led by voluntary mosquito control groups (such as secondary school, college, and university students) and local city/town/village/ward leaders/councillors should be enhanced. Earlier studies showed that mosquito control intervention in Bangladesh should start in April [6]. Finally, dengue vaccines are now available [13] and their effectiveness and safety require evaluation in field research and controlled trials for their role in the prevention of DENV transmission and the reduction of dengue-related morbidity and mortality.

The 2023 dengue outbreak in Bangladesh is a call for attention to dengue epidemic control, not just in Bangladesh but also in other endemic countries in South East Asia which have experienced surges of dengue cases amidst the COVID-19 pandemic. The scientific knowledge and the experiences from epidemic management in Bangladesh would be important in guiding dengue control strategies on a regional, if not global, level.

Conflicts of Interest

The authors declare no conflict of interest.

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Ethics statement

We used data that are publicly available in the daily press release of the Ministry of Health and Family Welfare (https://old.dghs.gov.bd/index.php/bd/home/5200-daily-dengue-status-report). In addition, we extracted the anonymized location data of the patients from the hospital registration through the Management Information System (MIS) of MoHFW. The coordinates of the patient's locations are approximate positions extracted from Google Sheet's add-ons 'Geocode by Awesome Table' and do not indicate the actual location of the case household. We obtained permission to use the patient's address to prepare maps as a part of the dengue outbreak response in Bangladesh.

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