Editor Comments to Author:  
  
Reviewer(s)' Comments to Author:  
Referee: 1  
  
Hasan et al reported the 2023 fatal outbreak of Dengue in Bangladesh and highlighting a paradigm shift of geographical distribution of cases.  
  
The manuscript is well-described, and materials and methods used are appropriate for this analysis.  
  
This reviewer noticed the description of festivals related cause in page 12, line 268-275.  
The religious festivals: Eid-Al-Fitr and Eid-Al-Adha, have been celebrating every year. Why did that of 2023 cause the large number of Dengue cases and high fatality rate of Dengue related death compared to those of previous years? Was there any associated factor? It should be discussed in the text.

Response: Thank you for your valuable time regarding this comment. The Eids of 2023—Eid al-Fitr and Eid al-Adha—differ significantly from previous years. Various climatic factors, such as early rains and ongoing construction projects by both the government and private sectors, alongside the lengthy holiday period during this rainy season, have contributed to the challenging situation. We discuss these factors in detail on page 12.

In page 12, “In recent years, the government and private sectors has initiated several large-scale construction projects, many of which are nearing completion. During this year's Eid vacation, the early onset of rain and the extended holiday period have resulted in many sites in the capital and surrounding areas becoming breeding grounds for Aedes mosquitoes, due to inadequate maintenance. Additionally, vacant houses and public spaces serve as ideal habitats for mosquitoes, allowing stagnant water from intermittent rains to accumulate without being cleared. Moreover, there is a lack of initiatives outside Dhaka to identify patients or remove these breeding sites.”  
  
  
  
Referee: 2  
  
  
(There are no comments.)  
  
Referee: 3  
  
  
The paper titled "The 2023 Fatal Dengue Outbreak in Bangladesh Highlights a Paradigm Shift in the Geographical Distribution of Cases" addresses a critical topic in dengue research, particularly concerning the severe epidemic in Bangladesh in 2023. However, several existing publications utilize the same data from the Bangladesh Ministry of Health and Family Welfare (MoHFH). This includes the paper by Rifa Tamanna Subarna and Zwad AI Saiyan, "Understanding the Unprecedented 2023 Dengue Outbreak in Bangladesh: A Data-Driven Analysis," IJID Regions (2024).  doi: <https://doi.org/10.1016/j.ijregi.2024.100406>.  
  
Subarna et al.'s paper uses data from the MoHFH, Bangladesh, covering the extensive period from January 2022 to December 2023, which includes detailed information on dengue patients from the 8 divisions of Bangladesh with comprehensive analysis. Given this context, it is important to clarify the unique contributions of your paper. Specifically, your paper does not extensively address climatic factors, viral factors, or genotypes associated with severe disease and fatal outcomes.  
Additionally, it would be beneficial if you could elaborate on the predictive factors for potential locations for future epidemics and the higher fatality rates in females, as well as provide recommendations for government actions. I would also appreciate it if the authors could explain Figure 2, specifically the reason for hospital stays of seven days or more. This information would greatly enhance the value of your research and distinguish it from existing studies.

Response: Thank you for this details comment. To assess the association of dengue cases in relation to climatic factors (daily average temperature, total daily rainfall, and average daily relative humidity) and showed in result and discussion part.

In results, page 10, we included, “Correlations were observed between monthly dengue cases and various meteorological parameters in the divisions of Bangladesh, including average temperature (r=0.13, p=0.032), total monthly rainfall (r=0.13, p=0.025), and average humidity (r=0.11, p=0.052).

In the GLMM, a statistically significant positive association was identified between the dengue cases and daily average temperature (IRR: 1.13, 95% CI: 1.11-1.14), daily average relative humidity of the division (IRR: 1.09, 95% CI: 1.08 – 1.09), urban and rural population ratio (IRR:1.04, 95% CI: 1.03-1.04). Daily total rainfall of the division (IRR: 0.99, 95% CI: 0.98-0.99), showed a significantly negative association between dengue cases. Population density and distance from Dhaka also exhibited weak negative associations **(Table 1)**.”

In discussion, page 13, we included, “We found a conflicting negative association between rainfall and dengue cases [25], which might be because of higher rainfall in the Sylhet division where the highest amount of precipitation is usually observed in Bangladesh. However, the relative humidity was positively associated with increased dengue cases in other countries including Thailand, the Philippines, and Sri Lanka [25].”

Due to limited data, we were unable to evaluate viral factors or genotypes associated with severe disease and fatal outcomes in our analysis. However, we discuss those in our limitations.

In page 13-14, “Our study has several limitations. The data we presented in this study has been recorded through hospital-based passive surveillance in Bangladesh [10]. The surveillance covers a mere fraction (5%) of the country’s total health healthcare facilities [1]. We do not have the circulating serotype data for the 2023 outbreak. However, several studies including WHO’s report on the Bangladesh dengue situation revealed that DENV- 2 which reappeared in the country in 2023, became a predominant serotype (62%) along with DENV-3 (29%), and co-infection of DENV-2 and DENV-3 (10%) [27,28]. Earlier, all four serotypes of the dengue virus have been recorded in Bangladesh at different times since 2000 [29,30]. DENV-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 [29].Thus, exposure to heterogenous serotypes in 2023 likely increased the risk of severe dengue infection which has a much higher CFR than the primary infection [21]. While we observed significant differences in dengue incidence and CFR between the southern and northern divisions, potential biases linked to the passive surveillance method cannot be ruled out. While improbable, there’s a chance that district health officials in the southern division may have reported more diligently than those in the northern divisions, despite the reporting system being the same throughout the country.”

Additionally, to assess the association of dengue cases in relation to potential locations and sex. We incorporate Urban-rural ratio and male-female ratio in the predictive model. However, in adjusted model male-female ratio not included due to insignificance of that variable. We included those association on results and discussion’s part.

Page 13-14, we added some recommendation, “To limit dengue virus infections in urban areas, particularly in Dhaka, it is crucial to regularly eliminate mosquito breeding sites and enhance surveillance for active cases. Continuous monitoring of dengue cases will facilitate early detection and help identify outbreak locations. Public health authorities can then take swift action to control mosquito populations, isolate infected individuals, and launch public awareness campaigns on preventive measures.

Both authorities and residents should avoid storing water at construction sites or in homes during vacation periods. Additionally, it’s important to remain vigilant about early rainfall and rising temperatures, which can increase mosquito populations. Developing a municipal water system to reduce the need for water storage is essential for preventing Aedes mosquito proliferation. Residents should not store water for extended periods and should change stored water regularly. Early detection and prompt response are key to preventing the spread of dengue and mitigating its impact.”

Referee: 4  
  
  
I read with interest a manuscript that addresses a topic which requires attention and a phenomenon that is worthwhile studying and following up going forward.  
I have few comments/suggestions and queries for edits and corrections:

• Introduction would benefit from few sentences at the start about Bangladesh population and Dengue spread in previous years, before 2023. Perhaps the second paragraph can go first.

Response: Najmul Bhai

• Statistical analysis section, lines 146/147: Using random effects to account for time series effects in the data, needs to be better explained. What time series? What was the time units?

Response: Thank you for your comments. We explained in better way.

In page 6-7, we added and modify some lines “The fixed effects (a measure of association), urban-rural ratio, male-female ratio, population density, distance from Dhaka (capital city), daily average temperature, daily total rainfall, daily average relative humidity was used to estimate the association between division-wise daily dengue counts (in number) and are expressed as an incidence risk ratios (IRRs) with a 95% confidence interval (CI). Regarding the measures of variation (random-effects), location with standard deviation (cluster) and intra-cluster correlation coefficient (ICC) were used. In addition, Akaike information criterion (AIC), Bayesian information criterion (BIC), Coefficient of determination (R2), and Root-mean-square error (RMSE) were used to report the variation of dengue cases at the division level and to test the model.”

• Statistical analysis section, lines 144/152, this part needs clarity. Please spell out, the outcome and the predictors used. Time series units of time and the justification for using the term time series rather than a generic longitudinal data. No interrupted time series models or any specific time series models were used.

Response: Thanks for you valuable time to provide this comment. The clarify our outcome and predictor variable that used in our model.

In page 7, we added, “In our model, outcome variables were used as counts variable of daily division-wise dengue cases in number and predictor variable as the urban-rural ratio (as an urbanization proxy), male-female ratio, population density, distance from Dhaka, and several weather factors. Variables with a p-value less than 0.05 in the final model were statistically significant determinants of dengue cases.”

We removed the term “time series data” and replace “longitudinal data”.

• Statistical analysis section, lines 150/151: adjusted incidence rate ratios (IRRs), considering dengue deaths: what is meant by considering dengue deaths, was the outcome death? Incidence of death? The sentence needs to be written clearly to explain what the outcome was and what was meant by considering. As it stands it is confusing and seems to suggest some confounders being considered or accounted for.

Response: “We mistakenly added the dengue deaths term, we check carefully now and remove deaths as our outcome variable is dengue case. In addition, we removed the term considered and rewrite the outcome and predictor variable clearly”

• Results, line 169-170: Although males constituted a higher percentage of cases (60 vs 40%), females constituted a greater proportion of deaths (57 vs. 43%); the latter two proportions are unclear, 43% of what? It was indicated earlier that the fatality rate was 0.53% in 2023. Do you mean 0.43%?

Response: Thanks for raising this issue, we incorporate it. To clarify the percentage, we rewrite the sentence. In addition, 43% is from total deaths not case fatality ratio. Where case fatality ratio is 0.53%, defined as the percentage of deaths divided by cases.

In page 8, we slightly change the previous line as “Although males constituted a higher percentage of cases (60 vs 40%) from total cases and females constituted a greater proportion of deaths(57 vs. 43%) from total deaths in 2023”

• Results, lines 178-179, stated that, “The average rainfall for the period 2000 to 2022 was 1915.75 mm whereas in 2023 total annual rainfall increased to 2160.70 mm”:  Using the average, assuming this is the arithmetic mean is not a good summary of rainfall over 23 years. A medina with upper and lower quartiles, would provide a better summary of the rainfall average, and range, within the period described.

Response: Thanks for find out our limitations. We added median with upper and lower quartiles.

In page 8, we modify, “The median rainfall for the period 2000 to 2022 was 1843.1 (IQR: 257.10) mm whereas in 2023 total annual rainfall increased to 2160.70 mm” and

“There was a similar range of temperature between 2023 and the period 2000-2022 (28.25 (IQR: 6.26) °C for the period 2000-2022 vs. 27.06 °C in 2023).”

• Line 186, (2.30 vs. 0.50) are these figures per 1000? Please be consistent in the way you report incidence per 1000 population and percentages. This was noted before. In only the sentence that follow-line 187- 2.9 was reported as per 1000. This is confusing.

Response: Thanks for the comments. We included per thousand population.

In page 8, we modify it as “The divisions southern to Dhaka had a higher dengue incidence compared to the northern division (2.30 vs. 0.50, p<0,0.01) per thousand population whereas the central Dhaka division had an incidence of 2.90 per thousand population.”

• Line 188, and relative humidity (80.79 vs. 79.08%) than the northern. Please complete the sentence, do you mean relatively higher?

Response: “We added “slightly higher”.

In page 8, “In 2023, the southern divisions recorded slightly higher annual temperatures (27.46 vs. 26.54 °C) and relative humidity also slightly higher (80.79 vs. 79.08%) than the northern division”

• Line 207 stated “There was a parallel trajectory in both Dhaka city and outside until mid-April”. Please edit the sentence for clarity, trajectory of what? And what do you mean by trajectory. Please explain.

Response: “We added “population”.

In page 9, “There was a parallel trajectory of population in both Dhaka city and outside until mid-April.”

• Lines 222/223 stated that “A similar association is evident between population density and dengue cases (r=0.47, p=<0.001) and deaths (r=0.43, p=<0.001) was the latter correlation of 0.43 between death and population density?

Response: Thanks for this comment.

We rewrite this sentence in page 10, “For monthly dengue cases and deaths, a positive correlation was observed between the population size of the district and the number of dengue cases (*r*=0.44, p=<0.001) and population size of the district and the number of dengue deaths (r=0.43, p=<0.001).”

• Figure 1. Please explain in title whether the number of dengue cases, and the number of deaths per month for the period 2000-2022 are totals or means?

Response: we added ‘total’.

• Figure 3. A. Please add units to time (X axis) it is not clear 0 to 300 what? Days?

Response: Asad Bhai

• Figure 3. second part is complex and should be simplified. A label should be added, is the second part B? for example. Relative changes may be presented in a table below the figure rather than adding an additional reference line to the figure.

Response: Asad Bhai

• Too many figures, some are not needed.

Response: Najmul Bhai

• Table 1, results, please add unadjusted IRRs.

Response: “We added unadjusted IRRs in Table 1”