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The Journal of Climate Change and Health

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Research article

Effects of diurnal temperature range on diarrhea in the subtropical megacity of Dhaka, Bangladesh



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ARTICLE INFO

Article History: Received 23 September 2023 Accepted 10 February 2024 Available online 16 February 2024

Keywords:
Diurnal temperature range
DTR
Diarrhea
Diarrheal diseases
Dhaka
Bangladesh

ABSTRACT

Introduction: While numerous studies have assessed the association of diarrhea with temperature, few have addressed the relationship between within-day variation of temperature and diarrhea.

Materials and methods: We investigated the association between diurnal temperature range (DTR) and daily counts of hospitalizations for all-cause diarrhea in Dhaka, Bangladesh using time series regression analysis employing distributed lag-linear models. Defining DTRs below 10th, 5th and 1st percentiles as low, very low and extremely low DTR, and DTRs above 90th, 95th and 99th percentiles as high, very high and extremely high DTRs, we additionally analyzed the effects of extreme DTR on diarrhea hospitalization. Effects were assessed for all ages, under-5 children and by gender.

Results: Although we did not find any significant effects of overall DTR and large DTRs, we detected significant effects of small DTRs on diarrhea hospitalization in all subgroups. A unit rise in low, very low and extremely low DTR was associated with a 4.9 % (95 % CI: 3.6 - 6.2), 7.1 % (95 % CI: 5.4 - 8.9) and 11.8 % (95 % CI: 8.3 - 15.5) increase in all-cause diarrhea hospitalization in all ages, respectively. A unit increase in low, very low and extremely low DTR was associated with a 4.9 %, 5.1 % and 18.4 % increase in all-cause diarrhea hospitalization in children under 5 years of age, respectively. The impact of extremely low DTR varied by gender (16.2 % in females versus 10.1 % in males). The effect of extremely low DTR was most pronounced in children under 5 years of age.

Conclusion: Less variation in within-day temperatures is a risk factor for diarrhea hospitalization in Dhaka, Bangladesh. Further research is needed to elucidate the causal pathways and identify the preventive measures necessary to mitigate the impacts of lowering DTRs on diarrhea.

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Introduction

Diurnal temperature range (DTR), defined as the difference between the maximum and the minimum temperature within one day, has attracted significant research attention in recent years [1]. DTR, regarded as an important meteorological parameter related to global climate change and urbanization, can reflect the stability of weather by incorporating information about maximum and minimum temperatures [1–5]. In the context of climate change, DTR is decreasing in many regions across the globe as nocturnal minimum temperatures are rising faster than daytime maximum temperatures [1]. Along with global climate change, the urban heat island (UHI) effect, in which urban areas maintain heat overnight, likely also contributes to the decreasing DTR. Despite the decreasing trend, some studies have shown that many people are still exposed to relatively large DTR for long periods of time [3,4].

Fluctuations of DTR can adversely affect human health, as the human body may be less capable of adapting to large variations of

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temperature and temperature range within a short period of time. A variable DTR is associated with cardiovascular events and even death [3,5] as well as affecting both cellular and humoral immunity [1] thereby potentially increasing people's vulnerability to infectious diseases. Abrupt changes in temperature can lead to pathophysiological responses of the respiratory epithelium triggering increased respiratory-related mortality or morbidity [1,6]. Sudden temperature change of inhaled air can release inflammatory mediators by mast cells causing an inflammatory nasal response [7] as well as increase the prevalence of gastrointestinal disease [8–10]. Intra-diurnal variation in temperature can trigger an increase in the levels of blood catecholamines and fibrinolytic parameters leading to strokes [1,11]. The effects of DTR on cardiovascular and respiratory mortality and morbidity have been investigated in many countries across the globe including Asia [1]. However, only a limited number of studies have looked into the effects of DTR on gastrointestinal morbidity including diarrhea [4,12].

Diarrhea remains a major cause of morbidity and mortality, particularly among children under 5 years of age despite the implementation of various vaccines against causative organisms in the low- and middle-income countries including in Bangladesh [13]. While the exact incidence of diarrhea is not available for Bangladesh, diarrhea is an endemic disease and a major cause of morbidity in the country [13]. According to the Bangladesh Demographic and Health Surveys (BDHS), the reported prevalence of diarrhea in the previous two weeks among under-five children was 5.7 % in 2014 [14]. Estimates from relatively smaller specific study populations at different time points in Bangladesh suggest that diarrhea mortality in children has declined significantly from 15.1 per 1000 in 1980 to 6.0 per 1000 live births in 2015 [14,15]. While Bangladesh has achieved significant success in reducing diarrhea mortality, outbreaks and hyper-endemicity continue to plague the nation despite notable improvements in socio-economic conditions as well as in water and sanitation infrastructure

Furthermore, many industrialized nations are struggling to control rotaviral diarrhea morbidity in children under 5 years of age [17]. A wide range of complex nutritional, socio-economic, cultural, behavioral and environmental drivers interact in the causation of diarrhea [18]. Despite the association of temperature with diarrhea, to date the impact of within-day variation in temperature on diarrheal diseases has not been thoroughly investigated. Heterogeneity exists among previous studies in terms of study designs, statistical methods, vulnerable groups, confounding factors, lag time and threshold of DTR [1,4,12]. Furthermore, only a few studies have examined the impact of extremely high and low DTR on human health [1,19]; and the role of potential confounders and effect modifiers on the relationship between DTR and human health is unknown [1].

This study aims to elucidate the relationship between overall and extreme DTR and hospitalizations for all-cause diarrhea and identify the modifying effects of age and gender on the DTR-diarrhea relationship in Dhaka Bangladesh.

Materials and methods

Study setting

Dhaka, the capital of Bangladesh with a tropical vegetation and moist lands, is a low-lying predominantly coastal city surrounded by rivers and water channels. This puts Dhaka at constant risk of flooding from rising sea levels [20–22]. With over 20 million residents, the rapidly expanding megacity is faced with several challenges including inadequate water supply and sanitation infrastructure and poor hygiene brought about by poverty [22,23].

Health data

Data of patients with all-cause diarrhea (defined as patients passing \geq 3 loose stools per 24 h due to any cause) were collected from the Dhaka Hospital of the International Centre for Diarrheal Diseases Research, Bangladesh (icddr,b). Icddr,b served approximately 14.6 million people and provided free treatment to more than 140,000 diarrhea patients in 2010 predominantly from urban Dhaka and its surrounding area. However, a few patients with severe diarrhea from outside Dhaka likely also seek care at Dhaka Hospital, which is a well-known diarrheal disease hospital [24,25]. The hospital is located within the city limits and near the largest land transport depot in Dhaka, which makes it geographically accessible to all city residents. However, healthcare-seeking data show that the Dhaka Hospital's services are accessed predominantly by disadvantaged groups and surrounding slum dwellers [26]. Given that reliable records of the total number of patients with all-cause diarrhea admitted per day or their dates of onset were not available for the study period (1981–2010), information from the robust Diarrheal Disease Surveillance System (DDSS) was obtained instead [25] to estimate the total number of diarrhea patients from Dhaka seeking care from the icddr,b Dhaka Hospital per day. The DDSS was established at the Dhaka Hospital in 1979 to study the epidemiological, clinical, and laboratory characteristics of a sample of the patients who came to the hospital for care each year. During 1981 and 1995, every 25th patient (4 % of the sample) and during 1996–2010, every 50th patient (2 % of the sample) was enrolled into the DDSS. After 2010, the hospital started maintaining electronic records of all admitted patients [24,26]. The investigators accessed data within the study period through 2010. Additional information on the health data, Dhaka Hospital and the DDSS is provided in *Appendix 1*.

Meteorological data

The meteorological data including daily data on maximum and minimum temperatures, relative humidity, and cumulative rainfall in Dhaka were obtained from the Bangladesh Meteorological Department (BMD) that recorded 3-hourly data from three validated weather stations across Dhaka. DTR was calculated by subtracting the daily minimum temperature from the daily maximum temperature. To explore the impacts of extreme DTR on diarrhea, six categories of DTR were generated as described in Table 1. The low, very low and extremely low DTR categories meant that there were very little within-day temperature fluctuations. On the other hand, high, very high and extremely high DTR categories meant that there were large variations of within-day temperature during these days.

Data analysis

Exploratory analysis

The 36 (0.33 %) missing entries in the DTR series and the 32 (0.29 %) days of missing health data were replaced by the monthly average for that parameter. The data series were checked for stationarity, autocorrelation, long-term trends, seasonality, normality, homoscedasticity

Table 1Definitions of categories of extreme diurnal temperature range (DTR).

| Extreme DTR categories | Definition |
|-------------------------------------|---|
| Extremely high DTR Very high DTR | A DTR ≥ 99th percentile during 1981 – 2010. A DTR ≥ 95th percentile during the study period. |
| High DTR | A DTR \geq 90th percentile during the study period. |
| Low DTR Very low DTR | A DTR ≤ 10th percentile during the study period. A DTR ≤ 5th percentile during the study period. |
| Extremely low DTR | A DTR \leq 1st percentile during the study period. |

and volatility using established methods. We used time series plots, seasonal and trend decomposition using Loess (STL), autoregressive moving average (ARIMA) and/or winsorization to detect and eliminate outliers in each data series if necessary [27–29]. Using autoregressive integrated moving average (ARIMA) model, the DTR data series were pre-whitened to achieve stationarity before checking cross-correlation with diarrhea data.

Statistical analysis

Time-series adjusted negative binomial regression models were used to quantify the acute effects of DTR and extreme DTR on diarrhea hospitalization. Given that past studies have identified mean temperature, relative humidity, day of the week, long-term time and seasonal trends as potential confounders on the relationship between DTR and various human health outcomes, the models were adjusted for these potential confounding factors [1,4,5]. The models were also adjusted for heavy rainfall (defined as the rainfall above the 95th percentile for the study period). A series of linear spline functions of time were used to flexibly model underlying trends and seasonal patterns unrelated to climate factors. The Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) and analysis of residuals were used to evaluate model fit and inform the choice of degrees of freedom for flexible splines.

Past studies have detected lagged effects of DTR on human health for up to lags of 27 days [5]. In addition, lagged effects of temperature, humidity and rainfall on diarrhea have also been reported previously [4,30]. Given that exploratory analysis revealed a linear relationship between DTR and diarrhea, generalized linear regressions combined with distributed lag linear models were employed to examine any delayed effects of each climate factor. Initially, the lagged effects of each climate factor were investigated separately and then simultaneously in an unconstrained distributed lag-stratified model. The final quantification of estimates was based on the model with all lagged climate variables entered simultaneously using a constrained distributed lag linear model that allowed overcoming the problem of collinearity leading to precise estimates of confidence intervals [31]. While the effects of DTR on diarrhea were detected for lags of up to 27 days, the lags of mean temperature, relative humidity and heavy rainfall were found to be negligible for lags above 7 days in this study.

The final model to investigate the lagged effects of DTR and other confounders on diarrhea took the following form:

 $Y_t \sim Negative Binomial(\mu_t, \theta)$

$$\begin{split} log[\textit{E}(\textit{Y}_t)] &= \beta_0 + \sum \beta_1 \textit{DTR}_{t-27} + \sum \beta_2 \textit{Temp}_{t-7} \\ &+ \sum \beta_3 \textit{Hum}_{t-7} + \sum \beta_4 \textit{Rain}_{t-7} + \sum \beta_5 \textit{dow} \\ &+ \sum \textit{LS}(\textit{Time}, 8) \end{split} \tag{1}$$

where Y_t denotes daily all-cause diarrhea hospitalization count, DTR_{t-27} denotes daily diurnal temperature range at lags 0 to 27 days, Temp_{t-7}, Hum_{t-7} and Rain_{t-7} denote the daily mean temperature, relative humidity and heavy rainfall at lags 0 to 7 days, respectively. To control for long term trends and seasonality, a flexible spline with 8 degrees of freedom per year was incorporated into the model. DOW_t denotes the categorical day of the week with a reference day of Friday. To control for residual autocorrelation, autoregressive terms at order 1 was incorporated into the model. All effect estimates were presented as incidence rate ratios.

To examine the effect of extreme DTR on diarrhea, different models were generated using the six indicators of extreme DTR.

The relative risk of hospitalization for all-cause diarrhea per unit change in DTR was calculated from Eq. (1) as incidence rate ratio (IRR) and the associated percentage increase in hospitalization were derived from the model parameters through Eq. (2).

$$\%change = 100(IRR - 1) \tag{2}$$

Multiple sensitivity analyses were carried by changing the amount of control for seasonality and long-term trends in the model (by using natural cubic splines and changing the number of knots in the spline-based approach). Further sensitivity analysis was conducted by including relative humidity as a linear term and heavy rainfall as a categorical variable without any lagged effects. In addition, the analyses were rerun using the total number of all-cause diarrhea patients enrolled into the icddr,b diarrhea surveillance platform (DDSS) as the outcome instead of the total estimated hospitalizations for all-cause diarrhea at the icddr,b Dhaka Hospital per day.

Results

There were an estimated 2,983,850 hospitalizations for all-cause diarrhea in the icddr,b Dhaka Hospital during the 30-year study period. Of these, 84,403 were enrolled into the DDSS platform. Among these, 58 % were males and 54 % were children under 5 years of age. The average values of the mean temperature and DTR were 25.9 (Range: 11.9-32.8) and $9.0\,^{\circ}$ C (Range: 7.8-10.1), respectively. The average relative humidity was $75.0\,^{\circ}$ K (Range: 31-99). The estimated median number of daily all-cause diarrhea admissions in all ages for the period was $250\,^{\circ}$ C(25th-75th percentile: 200-325) and in children under 5 years of age was $150\,^{\circ}$ C(25th-75th percentile: 100-200).

Fig. 1 shows the temporal distribution of DTR revealing a distinct seasonal pattern. Fig. 1 suggests that the variations of DTRs were lower during the months of June to September which corresponds to the monsoon season in Bangladesh. The variations of the DTRs were higher during the colder months of November through February. Fig. 2 shows the annual and Table 2 shows the monthly distribution of the six categories of extreme DTR. The total number of days per year with high, very high and extremely high DTR showed a decreasing trend across the decades. However, the total number of days with low, very low and extremely low DTR per year remained large. As shown in Table 2, days with low, very low and extremely low DTRs were observed throughout the year with the majority of the small DTR categories occurring between the monsoon months of June and October. On the other hand, high, very high and extremely high DTR categories were observed between the months of November and May only. Fig. 3 shows the relationships between low, very low and extremely low DTR and diarrhea hospitalization along the 27 lag days. Overall, the greatest effects of DTR on hospitalizations for allcause diarrhea were found at lag 0 with negligible effects observed until lags of 27 days.

Table 3 shows that a unit rise in low, very low and extremely low DTR was associated with a 4.9% (95% CI: 3.6 - 6.2), 7.1% (95% CI: 5.4)- 8.9) and 11.8 % (95 % CI: 8.3 - 15.5) increase in all-cause diarrhea hospitalizations in all ages, respectively. A unit change in low, very low and extremely low DTR were associated with a 4.9 % (95 % CI: 1.5 - 8.4), 5.1 % (95 % CI: 0.7 - 9.6) and 18.4 % (95 % CI: 8.8 - 28.9) increase in all-cause diarrhea hospitalizations in children under 5 years of age, respectively. The effects of low and extremely low DTR appeared to be greatest among children under 5 years of age whereas the effects of very low DTR was greatest among men. The impact of extremely low DTR varied by gender (16.2 % in females versus 10.1 % in males). While the detected effects of low and extremely low DTR were higher in females compared to males, the effect of very low DTR was found to be higher in males. However, no significant effects were detected for overall DTR and high, very high and extremely high DTR in any of the four groups. The sensitivity analysis conducted by changing the control for long-term trend and seasonality, modifying model parameters and by using total number of patients enrolled into the surveillance system instead of estimated counts of daily

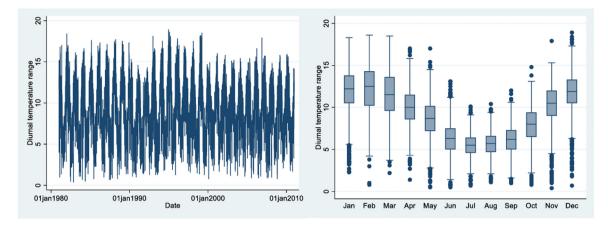


Fig. 1. The daily and monthly distribution of diurnal temperature range in Dhaka, Bangladesh from 1 January 1981 to 31 December 2010.

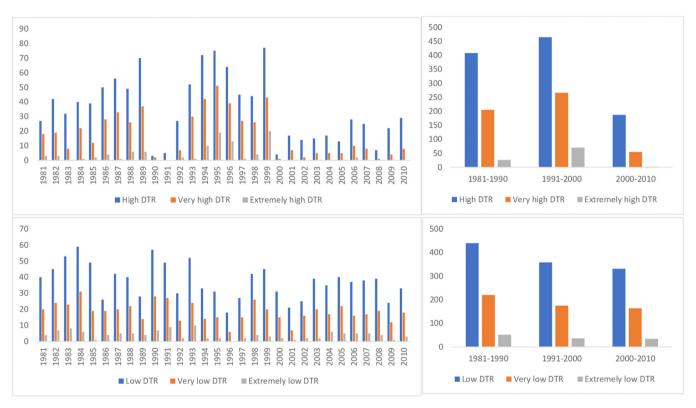


Fig. 2. Temporal distribution of categories of diurnal temperature range (DTR) in Dhaka, Bangladesh (1 Jan 1981–31 Dec 2010).

Table 2Monthly distribution of categories of extreme diurnal temperature range (DTR) in Dhaka Bangladesh during 1981 – 2010.

| Month | Number of days | | | | | | |
|-----------|-------------------|--------------|---------|----------|---------------|--------------------|--|
| | Extremely low DTR | Very low DTR | Low DTR | High DTR | Very high DTR | Extremely high DTR | |
| January | 0 | 14 | 23 | 272 | 136 | 20 | |
| February | 3 | 4 | 8 | 294 | 178 | 35 | |
| March | 0 | 5 | 9 | 236 | 140 | 36 | |
| April | 1 | 9 | 13 | 44 | 15 | 3 | |
| May | 8 | 24 | 42 | 14 | 4 | 1 | |
| June | 19 | 89 | 175 | 0 | 0 | 0 | |
| July | 13 | 103 | 245 | 0 | 0 | 0 | |
| August | 9 | 87 | 223 | 0 | 0 | 0 | |
| September | 23 | 90 | 174 | 0 | 0 | 0 | |
| October | 18 | 56 | 97 | 2 | 1 | 0 | |
| November | 9 | 21 | 31 | 61 | 7 | 1 | |
| December | 3 | 15 | 22 | 195 | 78 | 15 | |
| Total | 106 | 517 | 1062 | 1118 | 559 | 111 | |

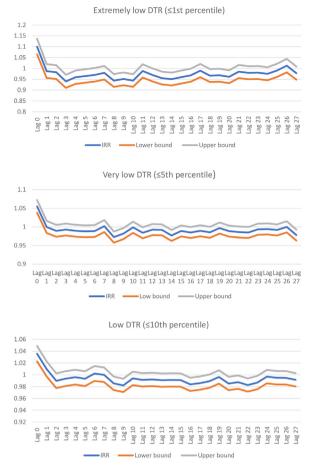


Fig. 3. Lagged effects of low, very low and extremely low diurnal temperature range (DTR) on diarrhea hospitalizations in Dhaka, Bangladesh.

diarrhea hospitalization as the primary outcome changed the results very little (Appendix 2).

Discussion

This study examined the effects of DTR on diarrhea hospitalizations in all ages and found no significant relationship between overall DTR and diarrhea after controlling for the confounding effects of mean temperature, relative humidity, heavy rainfall, long-term trend, seasonality, and day-of-the-week effect. In contrast to the findings of this study, a few past studies have reported linear and non-linear relationships between overall DTR and various health outcomes including diarrhea [1,3].

Although no significant effects of average DTR were detected, we identified significant effects of relatively small DTRs even after controlling for the effects of mean temperature in this study. Between 1981 and 2010, the population in Dhaka was exposed to low (<4.7 ° C), very low (<3.8 °C) and extremely low DTRs (<2.2 °C) for 1062, 517 and 106 days, respectively. Low, very low and extremely low DTRs were significantly associated with approximately 5 %, 7 % and 12 % increases in the risk of diarrhea hospitalizations in all ages, respectively. This suggests that less variability in within-day temperature, usually reflecting higher night-time temperatures, was a risk factor for diarrhea. However, the small DTRs were mostly clustered during the monsoon months of June through October. This suggests that additional epidemiological factors during monsoon that were not considered in this analysis also may have contributed to diarrhea hospitalizations. In contrast to past findings, this study did not find any significant effects of high, very high or extremely high DTR on diarrhea. A limited number of studies have reported greater effects of both extremely low and high DTR on health outcomes compared to average DTR [1]. Given that people were likely to take some protective measures during extremely high DTRs compared to lower DTRs, extremely low DTR may exert higher influence on diarrhea than extremely high DTR. Lou et al. (2013) reported greater effects of extremely low DTR on mortality than extremely high DTR [19]. Extremely low DTR may be associated with heat waves in summer and cold spells in winter. As a result, adverse health outcomes may be attributed to temperature without generating attention to the specific effects of lower DTR. In addition, climate parameters associated with small DTRs may affect the microbiological quality of drinking water as well as human behavior driving water consumption and hygiene practices that could then affect the incidence and/or hospitalization for diarrhea [32–35]. While identifying the exact pathways by which small DTRs lead to additional diarrhea incidence and/or hospitalization require further research, this study underscores the importance of raising awareness of patients, caregivers, medical, public health and allied staff of the particular high risk posed by relatively small DTRs on diarrheal disease morbidity among the residents of

In this study, the effects of low, very low and extremely DTR on diarrhea were found to be acute with the greatest effects observed on the same day (lag 0) with negligible effects observed for up to 27 lag days. Prior studies exploring the lagged effects of DTR on various health outcomes have reported various lag days from the same day (lag 0) of exposure to 27 days [1,19]. Xu et al. (2013) reported the greatest effect of DTR on childhood diarrhea at one day lag [4]. Wen et al. (2015) reported greatest effect of DTR on bacillary dysentery at 1-day lag [12]. In contrast, DTR effects were greatest at lag 3 for sudden infant death (SID) and at lag 5 for chronic obstructive pulmonary disease (COPD) mortality [1,36]. The variability in the biological mechanisms by which DTR influences disease causation may partly explain the variation observed in the time period between DTR

Table 3Percentage increase in all-cause diarrhea hospitalization associated with one unit increase in diurnal tempearture range (DTR) on the same day in Dhaka, Bangladesh.

| DTR category | Percentage increase (95 % CI) | | | | | |
|--|---|--|--|--|--|--|
| | All ages | Under-5 children | Males | Females | | |
| DTR (°C) Extremely low DTR (≤2.2 °C) Very low DTR (≤3.8 °C) Low DTR (≤4.7 °C) High DTR (≥13.6 °C) Very high DTR (≥14.7 °C) Extremely high DTR (≥16.5 °C) | 0.18 (-0.04 - 0.41) 11.83 (8.27 - 15.51) 7.14 (5.44 - 8.88) 4.85 (3.56 - 6.15) -1.82 (-3.25 - 0.38) -2.15 (-3.96 - 0.30) -1.50 (-5.12 - 2.26) | 0.02 (-0.56 - 0.61) 18.43 (8.83 - 28.87) 5.08 (0.74 - 9.62) 4.88 (1.52 - 8.35) -2.03 (-5.72 - 1.80) -0.05 (-5.29 - 4.43) -1.79 (-11.07 - 8.47) | 0.07 (-0.50 - 0.64) 10.14 (1.48 - 19.53) 8.44 (4.11 - 12.96) 4.70 (1.46 - 8.05) -3.50 (-7.02 - 0.16) -0.07 (-10.98 - 2.12) -5.17 (-13.85 - 4.39) | 11.34 (-1.43 - 25.77) 16.23 (3.06 - 31.09) 4.86 (0.04 - 11.36) 4.84 (0.08 - 9.83) 0.85 (-4.56 - 6.58) 2.51 (-4.45 - 9.97) 8.32 (-5.94 - 24.75) | | |

Bold values significance was defined as P-value < 0.05.

exposureand different health outcomes. The results of lagged association were inconsistent in different studies and varied by health outcomes and geographic location [1]. Therefore, the result of this study should only be generalized to other diseases or target populations with caution.

While the exact mechanisms by which exposure to low, very low and extremely low DTR influence the risk of diarrhea in young children remain largely unknown, children under 5 years of age were observed to suffer greater impacts of small DTRs compared to all ages in this study. It has been suggested that compared to other age groups, children may be more vulnerable to the health impacts of DTR overall. Sudden within-day variation of weather conditions may affect humoral and cellular immunity as well as lead to release of inflammatory mediators by mast cells contributing to diarrhea [7,9,10,37]. In addition, the immune system in children is likely to be immature [4,38]. Furthermore, children are likely to exhibit low self-care capacity [39]. In a previous study, Xu et al. (2013) reported significant association between DTR above 10 °°C and childhood diarrhea [4], which was not found in the current study.

In this study, females were found to be at higher risk of diarrhea hospitalization due to low and extremely low DTR compared to males. However, the result was inconsistent for very low DTR where males appeared to face a greater risk of diarrhea compared to females. Past studies that have examined how gender variations affect the vulnerability of health outcomes to the impacts of DTR have reported inconsistent patterns in both males and females [4,40,41]. For example, Kan et al. did not find any statistically significant difference of the impact of DTR on mortality in Shanghai, China between the two genders [42]. In contrast, Yang et al. (2013) and Lim et al. (2012) found that women were more sensitive to the cumulative effects of DTR with regards to total and cardiovascular mortality [3,43]. However, effects of temperature on morbidity among males and females could vary among different locations and populations due to immunological differences [40,44], and variations in body composition, sexual dimorphism and social behavior between males and females could lead to different disease risks [4,45,46]. Xu et al. (2013) found a more prolonged risk of high DTR on female children with diarrhea compared to male children [4]. Future studies should focus on identifying the biomarkers affected by DTR to shed light on the observed variations in mortality and morbidity by age groups and

While this study used advanced statistical techniques to quantify the immediate and lagged effects of DTR and extreme DTR on all-cause diarrhea hospitalizations and further examined the variations of DTR impact by gender and age groups, this study has several limitations. First, the study used estimated data from one hospital in one city given that reliable records were not available and/or accessible from other hospitals in Bangladesh. However, this does not compromise the validity of the results of this study, which is to compare DTR-diarrhea relationships over time. Furthermore, there is no reason to expect the effects of DTR to vary significantly in patients from Dhaka seeking care from hospitals other than icddr,b Dhaka Hospital. However, the generalizability of the results to other countries and rural areas may be inappropriate given that diarrhea risk is also determined by socio-economic factors, availability of WASH interventions and human behavior. Secondly, because individual exposure data were not available, the use of aggregate environmental data likely introduced exposure misclassification bias. In addition, individual level factors that likely also modify the impacts of DTR on diarrhea could not be analyzed in this study, as only group data were accessible. However, the time series design that was adopted in this study is rarely affected by normal confounders, such as differences in socio-economic status, which typically only change relatively slowly over time [27]. Lastly, a small number of diarrhea cases may have been admitted twice during the 28 days of the lag period considered in this study and a few cases may have been underreported, which likely introduced some bias.

Conclusion

With ongoing climate change, DTRs are likely to become more and more divergent from historical patterns [47,48]. The effects of lowering DTRs on diarrhea are likely to become more severe, particularly among children under 5 years of age and females. These findings underscore the importance of conducting research to elucidate the impacts of DTR on diarrhea as well as to develop targeted health policies and programs to mitigate the risks.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical approval

This study was granted approval by the Research Review Committee (RRC) and Ethical Review Committee (ERC) of icddr,b (PR-19,097). The study used secondary data and did not involve primary data collection from human participants. The study was also approved by the UCL Research Ethics Committee (UCL REC).

Informed consent statement

Patient consent was waived due to no individual data being collected.

Data sharing/availability statement

According to institutional data policy of the icddr,b (International Centre for Diarrhoeal Disease Research, Bangladesh), only summary of data can be publicly displayed or can be made publicly accessible. To protect intellectual property rights of primary data, icddr,b cannot make primary data publicly available. However, upon request, Institutional Data Access Committee of icddr,b can provide access to primary data to any individual, upon reviewing the nature and potential use of the data. Requests for data can be forwarded to: Ms. Armana Ahmed, Head, Research Administration, icddr,b, Dhaka, Bangladesh, Email: aahmed@icddrb.org, Phone: +88 02 9,827,001–10 (ext. 3200).

Author agreement

This is to certify that all authors have seen and approved the final version of the manuscript being submitted. I confirm that the article is the authors' original work, hasn't received prior publication and isn't under consideration for publication elsewhere.

Farhana Haque

Corresponding author, on behalf of all co-authors

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Farhana Haque: Writing — review & editing, Writing — original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Fiona Lampe:** Writing — review & editing, Supervision, Methodology. **Shakoor Hajat:** Writing — review & editing, Supervision, Methodology. **Katerina Stavrianaki:**

Writing — review & editing, Supervision, Methodology. **ASG Faruque:** Writing — review & editing, Project administration, Data curation. **Shamim Jubayer:** Writing — review & editing, Project administration, Data curation. **Ilan Kelman:** Writing — review & editing, Supervision, Resources, Methodology, Conceptualization. **Tahmeed Ahmed:** Writing — review & editing, Supervision, Resources, Project administration, Data curation.

Acknowledgements

This study was completed as a part of a PhD thesis by FH. The authors would like to thank the Commonwealth Scholarship Commission for funding the PhD study. The authors are grateful to the members of the Research Administration team of icddr,b, National Health Foundation and Research Institute (NHF&RI) and Bangladesh Meteorological Department (BMD) for their support to data collection.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.joclim.2024.100305.

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